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Effects of different exercise modalities on oxygenation stress, inflammatory factors, and drug craving in drug users during the audit period

Shunjie Wu, Yanmei Chen

College of Physical Education, Southwest University, Chongqing, China

Shunjie Wu: male, master's degree, research interests: exercise monitoring

Email: 1050568774@qq.com

Orcid：https://orcid.org/0009-0005-4110-2059

Corresponding author:

Yanmei Chen: Female, Associate Professor, School of Physical Education, Southwest University, Research Interests: Exercise Monitoring, Exercise and Drug Rehabilitation

Email：83533757@qq.com

Orcid：https://orcid.org/0009-0001-1566-3822

Abstract

Purpose: The relationship between drug addiction and oxidative stress and inflammatory factors has not been clearly established. Drugs can induce oxidative stress as well as inflammatory reactions in the organism, disrupting inflammatory homeostasis, which is one of the mechanisms by which drug-dependent people develop drug craving. We investigated the effects of different exercise modes on oxidative stress, inflammatory factors and drug craving in drug addicts during the audit period**, and** explored the biological mechanisms by which exercise reduces drug craving craving from the perspective of inflammation in the body . **Subjects and methods:** A random sampling method was used to include 40 female drug addicts who met the criteria from a drug rehabilitation centre, divided into a yoga group (n=10), a meditation group (n=10), a physical fitness group (n=10), and a control group (n=10), and underwent a 12-week intervention training 3 times a week for 1 h each time. Serum concentrations of MDA, HCY, TNF-α, IL-6, IL-1, and ICAM-1 were detected in subjects before and after the intervention; and drug craving was assessed using a visual analogue scale (VAS). **RESULTS:** (1) Oxidative stress and inflammation levels were elevated in female drug users during the audit period compared to healthy individuals ; (2) After 12 weeks of exercise intervention, blood MDA, HCY, **TNF-α**, ICAM-1, IL-6, and IL-1 levels were decreased in the yoga, meditation, and physical fitness groups ($p<0.05$); and (3) the VAS scores in the yoga, meditation, and physical fitness groups were significantly reduced (p&lt ;0.01). **Conclusion**: (1) The levels of oxidative stress and inflammatory factors were elevated during the audit period in female drug addicts, and there was an inflammatory response in the body; (2) 12 weeks of meditation, yoga and physical fitness training could significantly reduce the levels of oxidative stress and inflammation in drug addicts, and contribute to the formation of inflammatory homeostasis. (3) All three types of exercise can reduce drug craving to a certain extent.

Keywords: exercise; drug users; inflammatory factors; drug craving

Introduction

Drug addiction is a chronic brain disease in which the brain's neurotransmitters, such as dopamine and glutamate, are altered, leading to an imbalance in the reward system, and interactions between drugs and the immune system lead to oxidative stress and the development of neuroinflammation in the brains of drug users [1] . **Existing research suggests that oxidative stress and inflammatory responses are key factors in the development and maintenance of substance use disorders, and that the mechanism is that (drug) substance abuse causes activation of neural microglia, which activates their inflammatory cascade response, releases inflammatory factors, triggers neuroinflammation, and maintains the onset of drug craving and relapse behaviours, in an infinite loop** (e.g., Fig. 1) [2-6] , and **that this mechanism has been both experimentally in animals and in humans have been confirmed.** Repeated administration or long-term exposure to chronic cacodyne resulted in elevated levels of TNF-α, IL-6 and CCL2 in the brains of mice [7-9] ; Eidson et al, Clarissa Catalea et al. Acute administration of high doses of morphine to mice resulted in elevated peripheral or central nervous system concentrations of IL-10, IL-1β, TNFα, IL-6, and Increased TNF-α and I-L6 gene expression in microglia, whose lack of pleasure is related to defective expression of inflammatory genes [10] ; Yang Ting Jade et al. have also demonstrated that methamphetamine (METH) induces NF-κB activation in the microkeratinocytes of the mouse brain, leading to increased secretion of the inflammatory factors IL-1β, TNF-α and IL-6. Thus either **acute or chronic** exposure to drugs activates microglia TLR-4 expression ,leading to high expression of central or peripheral blood inflammatory factors and correlates with the severity of withdrawal behaviour [11].

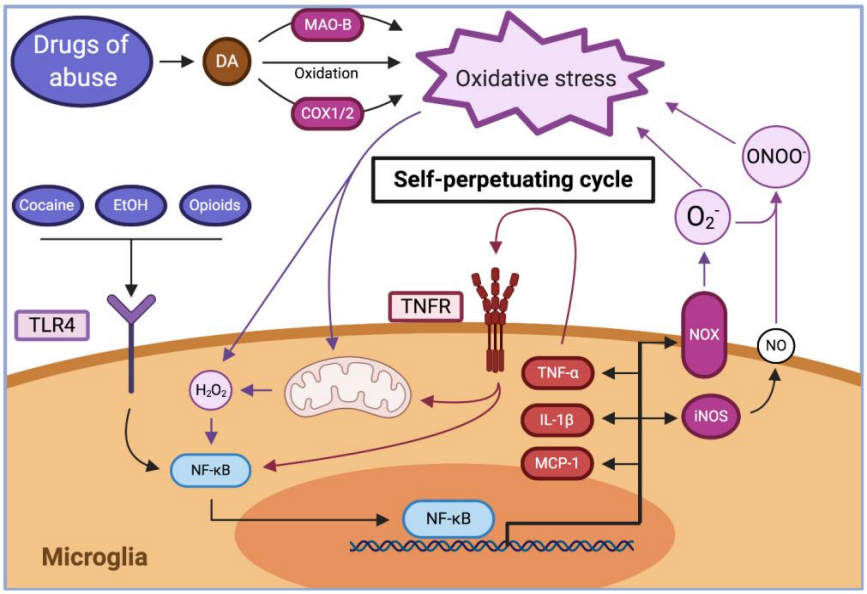


Figure 1: Substance abuse increases levels of oxidative stress and inflammation in the brain and triggers a self-perpetuating cycle that maintains neuroinflammation.
Graphic from BACHTELL R, et al,2015.Targeting the Toll of Drug Abuse: The Translational Potential of Toll-Like Receptor 4. CNS Neurol Disord Drug Targets.

Clinical experiments have also shown that either acute or chronic drug use leads to changes in the levels of oxidative stress and inflammatory factors in drug users at different stages. For example, Michael J. Lia,b, Marisa S. Brionesa et al. showed an increase in sICAM-1, sVCAM-1 and histone D 60 minutes after **acute treatment** with MET in volunteers, and a significant increase in IL-6 360 minutes after METH infusion; . Moreira, Levandowski, Alvaro Morcuende et al. showed in the study of persons **in the drug abuse period**: a decrease in IL-10 and an increase in IL-6, IL-1β, TNFα, CRP, SOD, and MDA in their peripheral blood; and the results of the study of persons **in the withdrawal period of** drug abuse by Maza-Quiroga and Pedraz showed a decrease in the concentration of IL-17, MIP-1α, and TGF-α, and a decrease in the concentration of TNF-α, 8- OHdG, LPS, CRP, IL-6 / I L-10 elevated [13] ; Walker et al. demonstrated: enhanced oxidative damage and significantly lower antioxidant capacity in methamphetamine-dependent patients compared to healthy controls. **In conclusion:** long-term use of cannabis, cocaine, opioids, and methamphetamine leads to elevated levels of MDA, IL-6, IL-6/IL-10, IL-1β, TNFα, and ICAM-1 in the peripheral blood of subjects, and is closely associated with cognitive decline and anxiety-depressive states during withdrawal, maintaining a vicious cycle of addictive and relapsing behaviours [14, 15] ; **there are also Different results have been reported:** for example, Halpern, Gupta et al. demonstrated that acute administration of cacodyne led to a decrease in IL-6 concentration in peripheral blood in humans, and that the reason for the contradictory results may lie in the fact that subjects were in different stages of drug treatment, such as withdrawal and relapse [16, 17] .

Exercise has been widely studied and valued as a green therapy to assist in drug rehabilitation. Exercise training can produce a good adaptation of the body's antioxidant enzyme system, protect the body from oxidative damage caused by free radicals to biological macromolecules, prevent the destruction of the blood-brain barrier, promote its reconstruction, reduce the body's oxidative stress and inhibit the expression of inflammatory factors, thus affecting the function and stability of the immune system [18-24] .

Animal experiments on exercise therapy have shown that appropriate exercise can improve the antioxidant capacity of the hippocampus, reduce the neurotoxicity of its microvascular system, and ameliorate the damage of METH to the blood-brain barrier in mice. Specifically, exercise can increase the activity of CAT enzyme in the hippocampus of mice, restore the integrity of the blood-brain barrier, reduce the concentration of MDA, IL-1β, TNF-α, IL-6 in peripheral blood, reduce drug craving, and produce a long-lasting protective effect on addicted animals.([23, 25-29]) .

Studies on the effects of exercise on drug users show that: regular aerobic exercise can reduce the level of oxidative stress and inflammatory factors in the blood of drug users, reduce the concentration of IL-1β, TNF-α, IL-6 in the blood, and the concentration of cytokines IL-17, IL-9, IL-19 undergoes benign changes; the metabolism level of the inflammatory pathway canine uric acid is lowered, and at the same time, it changes the cognitive level of the brain of the drug user , anxiety-depressive state as well as drug craving [12,30-33] . Although aerobic exercise can reduce oxidative stress and chronic inflammation in the body, there are fewer studies on the anti-inflammatory and detoxification effects of different types of exercise. Due to the long-term lack of exercise in the majority of SUD patients, their level of health is lower than that of the general population, and they are difficult to withstand strenuous exercise loads. Yoga and meditation, due to the lower intensity of their exercises, which involves a combination of body postures and breathing, are able to reduce perceived stress, anxiety, depression, inflammation, enhance brain connectivity, and promote drug addiction. Yoga and meditation can reduce perceived stress, anxiety, depression, inflammation, improve brain connectivity, promote dopamine homeostasis in drug users, and provide long-term benefits for addictive behaviours in the "reward deficit syndrome", thus reducing drug cravings and achieving the same effect as aerobic exercise.([34-38]) .

The current literature on the effects of drug craving in drug users from the perspective of oxidative stress and inflammatory factors through yoga and meditation interventions has not been reported. Based on the above, the present study used three modes of aerobic exercise, yoga and meditation to monitor the changes of MDA, HCY,

ICAM-1, IL-1, IL-6, TNF-A concentrations in the blood of drug abusers during the withdrawal period and the changes of drug craving, with a view to seeking the optimal model of intervention and providing a theoretical basis and a practical foundation for a better intervention for drug abusers. This study is a randomised controlled experiment, divided into an exercise group and a control group, using three forms of exercise: aerobic exercise, yoga, and meditation, three times a week, 60 minutes each time, with a training cycle of three months, and testing various indicators and drug craving before and after the training, to explore the independent therapeutic effect on drug addicts.

Hypothesis:

(1) The level of oxidative stress in drug addicts during detoxification and the level of inflammation in the body is higher than in normal healthy people;

(2) Aerobic exercise, yoga, and meditation have the effect of reducing inflammation and drug cravings in the body;

(3) There is a linear relationship between drug craving and body inflammation.

1. Experimental objects and methods

1.1 Experimental Objects

Using a random sampling method, 40 drug addicts were randomly selected from Chongqing Compulsory Isolation Drug Rehabilitation Center from 5 August to 8 November 2019 and divided into 4 groups, namely, yoga group (n=10), meditation group (n=10), physical fitness group (n=10), and control group (n=10), and no drug addicts withdrew throughout the experiment. Inclusion criteria: 1) aged 18-50; 2) completed the physical detoxification stage and entered the physical rehabilitation stage; 3) no history of mental illness, no hallucinations, delusions, thought disorders and other psychiatric symptoms, no cardio-cerebral and cerebral vascular diseases, infectious diseases, diseases of the haematopoietic or endocrine system, metabolic disorders, contraindications to exercise, etc., due to physical illnesses that can not participate in sports; 4) no anti-inflammatory drugs in the last three months; 5) voluntary enrolment, and no withdrawal of drug users throughout the experimental period. (5) Voluntary enrolment, with a guarantee of 3 months of presence in order to complete the study.

Ethical approval: Ethical approval for this study was obtained from the Medical Ethics Committee and the study was completed in accordance with the ethical requirements for clinical trials. Each study subject signed an informed consent form. The principle of

confidentiality was applied to the basic information of all study subjects, and all study data were not allowed to be disclosed to the outside except for the members of the subject group. During the course of the study, the research subjects have the right to withdraw from the study at any time for their own reasons.

1.2 Campaign programme

1.2.1 Physical training exercise programme

Table 1: Aerobic Fitness Exercise Programme

Exercise prescription variables	Specific content and requirements
sports format	Aerobic endurance, agility and flexibility, small load strength training
exercise frequency	3 times per week
exercise duration	60 minutes each time.
exercise intensity	Adjusted to 50% maximum heart rate in the early stages, gradually increasing to 70-80% later on
training cycle	12 weeks

1.2.2 Yoga exercise programme

Table 2: Yoga exercise programme

Exercise prescription variables	Specific content and requirements
sports format	yoga (loanword)
exercise frequency	3 times per week
exercise duration	60 minutes each time.
exercise intensity	Small to medium intensity asana training for the first 3 weeks, moderate intensity sequential asana training for weeks 4-12
training cycle	12 weeks

1.2.3 Meditation programme

Table 3: Meditation Training Programme

Exercise prescription variables	Specific content and requirements
element	contemplation
Training frequency	3 times per week
training time	60 minutes each time.
Organisation of the process	Basic meditation practice for the first 1-3 weeks, brain training and will exercise in the face of addiction for 4-12 weeks
training cycle	12 weeks

1.3 Blood collection and testing

1.3.1 Blood collection and processing:

At 8:00 a.m. in the morning before and 8:00 a.m. in the morning of the next day after the intervention, 5 ml of venous blood was withdrawn on an empty stomach, left for 30 min, centrifuged at 3,000 r/min for 15 min, and then serum was extracted and stored in a refrigerator at -80 ℃ for testing. 100 μL of serum from each of the pre- and post-intervention days was then used for the sample testing.

1.3.2 Test Methods;

Main reagents: ELISA test kits from Shanghai Yubo Biotechnology Co., Ltd (2) Main instruments and consumables, enzyme labeller: products from Finland; plate washer: products from Finland; centrifuge: micro high-speed centrifuge (domestic); pipette: Gilson P pipette products.

1.3.3 Experimental steps

Dilution and spiking of the standard: the standard was diluted into five gradients according to the instructions, and each gradient was spiked with 50ul of sample per well;

②Sample addition: set up blank wells and sample wells to be tested respectively. Add 40ul of sample diluent to the wells of the sample to be tested, then add 10ul of the sample to be tested. add the sample to the bottom of the wells of the plate, try not to touch the walls of the wells, and shake gently to mix;

(iii) Warming: seal the plate with sealing film and then place it at 37℃ for 30min;

④Washing with liquid: Dilute 30 (20 times of 48T) times concentrated washing solution with distilled water 30 (20 times of 48T) times and prepare for use; carefully remove the sealing membrane, discard the liquid, shake dry, fill each well with washing solution, leave it for 30sec and then discard it, and so on for 5 times, pat dry;

⑤ Add enzyme: add 50ul of enzyme reagent to each well, except the blank well;

(vi) Warming: seal the plate with sealing film and then place it at 37℃ for 30min;

(vii) Wash: carefully remove the sealing film, discard the liquid, shake dry, fill each well with washing solution, leave for 30sec and discard, repeat this 5 times, pat dry;

⑧Colour development: add 50ul of colour developer A to each hole, and then add 50ul of colour developer B. Shake gently and mix well, and then develop the colour at 37℃ for 15min away from light;

⑨ Termination: add 50ul of termination solution to each well to terminate the reaction;

⑩Assay: Measure the absorbance (OD) of each well sequentially at 450nm with a blank air-conditioner zero. Measurement should be carried out within 15min after adding the termination solution.

1.4 Tests of drug cravings

Drug craving is measured using a subjective self-reported, primarily visual analogue scale (VAS), which requires subjects to present a 10-cm horizontal line on a 0-10 numerical axis, divided equally into ten cells, in the centre of a VAS scorecard or computer. The left end of the line is 0, which indicates that the drug is "not wanted at all" (no craving) at the present moment; the right end is 10, which indicates that the drug is "wanted very much" (extreme craving); and the middle portion of the line indicates varying degrees of drug craving. Prior to the test, subjects were presented with an addiction cue-evoking stimulus consisting of a picture of the drug, the drug paraphernalia, and the drug scene, after which they were asked to respond to the question "Right now, how much do I want the drug?". , and to draw a line as a mark on the horizontal line to indicate the level of craving for the drug according to the subjective self-feeling in the present moment, as required by the instructions. In addition, the VAS assessment of drug dependent people's craving for addictive drugs has been confirmed by numerous studies with high reliability and validity.

Now, I'm thirsty for meth to the point of
0 expresses not wanting it at all, 10 means wanting it very much, and the higher the number, the higher the level of desire.

Figure 2:Example of a Visual Analogue Scale (VAS) to measure immediate craving
Graphic from "Theory and Application of Exercise to Promote Rehabilitation of Drug Dependence Disorders" by Chenglin Zhou and Dongshi Wang.

1.5 Statistical methods

The data obtained were statistically analysed using SPSS 25.0. Indicators that conformed to normal distribution and chi-square in data processing were expressed as mean ± standard deviation (M ± SD), and vice versa as median (P25, P75) [M (P25, P75)], with data accurate to two decimal places. Basic demographic characteristics were determined using descriptive statistics, one-way ANOVA ANOVA, and non-parametric tests Kruskal-Wallis-H test. The paired-samples t-test was used to compare the data before and after the experiments of the four groups. One-way ANOVA was used to compare the data between groups, during which the Bartlett's test for positive distribution and chi-square was performed first, followed by one-way ANOVA, LSD for post hoc test, and Bonferroni for correction of P-value, with $P < 0.05$ indicating significant difference, and $P < 0.01$ indicating highly significant difference.

2. Experimental results

2.1 Basic demographic characteristics of subjects

No subject dropped out of the 12-week exercise intervention, and the completion rate of the exercise group (yoga group, meditation group and physical fitness group) and the control group was 100%. After normal distribution and variance chi-square test for the basic characteristics of the subjects, the indicators of age, height and body mass conformed to the parametric test with one-way ANOVA test (F), and the suitability of years of drug use, withdrawal time and number of forced isolation with the non-parametric test Kruskal-Wallis-H test (H). Statistical analyses showed no significant differences in the basic demographic characteristics of the subjects.

Table 4: Demographic characteristics of the subjects

	variant	Yoga group (n=10)	Meditation group (n=10)	Physical fitness group (n=10)	Control group (n=10)	F/H	P
	Age/years	31.60±5.12	32.10±7.49	30.6±5.46	32.80±6.49	0.22	0.88
	Height/cm	159.90±6.80	159.9±3.90	158.30±4.80	161.80±4.98	0.74	0.53
	Body mass/kg	54.20±6.01	54.10±5.91	53.80±4.91	55.40±5.54	0.15	0.92
educational attainment	secondary schools	1 (10%)	2 (20 per cent)	2 (20 per cent)	1 (10%)	0.47	0.70
	junior high school	5 (50 per cent)	4 (40 per cent)	6 (60 per cent)	6 (60 per cent)		
	congrats! (on passing an exam)	3 (30 per cent)	3 (30 per cent)	2 (20 per cent)	3 (30 per cent)		
	University and above	1 (10%)	1 (10%)	0 (0 per cent)	0 (0 per cent)		
careers	out of work	5 (50 per cent)	4 (40 per cent)	4 (40 per cent)	3 (30 per cent)	0.40	0.93
	peasants	0 (0 per cent)	0 (0 per cent)	1 (10%)	1 (10%)		
	worker	0 (0 per cent)	4 (40 per cent)	1 (10%)	1 (10%)		
	Services	3 (30 per cent)	0 (0 per cent)	2 (20 per cent)	3 (30 per cent)		
	self-employed person	2 (20 per cent)	1 (10%)	2 (20 per cent)	0 (0 per cent)		
	the rest	0 (0 per cent)	1 (10%)	0 (0 per cent)	2 (20 per cent)		
matrimonial	unmarried	6 (60 per cent)	6 (60 per cent)	7 (70 per cent)	5 (50 per cent)	1.87	0.59
	married	4 (40 per cent)	3 (30 per cent)	3 (30 per cent)	2 (20 per cent)		
	divorced from (one's spouse)	1 (10%)	1 (10%)	0 (0 per cent)	3 (30 per cent)		
Type of drug	methamphetamine	6 (60 per cent)	7 (70 per cent)	7 (70 per cent)	6 (60 per cent)	1.12	0.77
	methamphetamine	1 (10%)	0 (0 per cent)	1 (10%)	0 (0 per cent)		
	heroin (loanword)	1 (20 per cent)	0 (0 per cent)	1 (10%)	2 (20 per cent)		
	ketamine (slang)	2 (20 per cent)	1 (10%)	1 (10%)	2 (20 per cent)		
	Drug use (g/dose)	0.65±0.27	0.61±0.20	0.55±0.20	0.59±0.24	0.31	0.81
	Frequency of drug use (days/week)	4.50±1.35	4.20±2.14	4.40±1.71	4.30±1.63	0.05	0.98
	Years of drug use	5.5 (5,9)	5.5 (5,9)	6(5,9)	5.5 (4,12)	1.03	0.79
	Phase time/month	7.5 (6,9)	7.5 (7,9)	8.5 (6,10)	8(6,10)	0.03	0.97
	Number of mandatory segregations	1(1,2)	2(1,3)	1(1,2)	1(1,2)	2.14	0.54
cigarette smoking	be	4 (40 per cent)	3 (30 per cent)	2 (20 per cent)	5 (50 per cent)	2.14	0.54
	clogged	6 (60 per cent)	7 (70 per cent)	8 (80 per cent)	5 (50 per cent)		
drinking wine	be	7 (70 per cent)	8 (80 per cent)	8 (80 per cent)	6 (60 per cent)	1.34	0.71
	clogged	3 (30 per cent)	2 (20 per cent)	2 (20 per cent)	4 (40 per cent)		

2.2 Effect of different exercise modalities on blood oxidative stress levels in female drug users

2.2.1 Within-group comparison of different exercise modalities on MDA and HCY in female drug users

Table 5: Within-group comparison of different exercise modalities on MDA, HCY among female drug users

groups	norm	pre-testing	post-test	(number of) degrees of freedom (physics)	T	P
meditation group	MDA	4.15±0.96	2.26±0.82**	9	-5.583	0.000
	homocysteine (Cys), an amino acid	16.74±2.27	12.61±2.69**	9	4.547	0.001
yoga group	MDA	4.20±1.17	1.76±0.98##	9	-6.037	0.000
	homocysteine (Cys), an amino acid	15.67±2.35	12.08±2.75##	9	3.733	0.005
fitness group	MDA	3.07±1.15	2.40±0.93&	9	-2.787	0.021
	homocysteine (Cys), an amino acid	15.70±2.84	12.62±2.94&	9	2.672	0.026
control subjects	MDA	4.05±0.76	3.97±1.08	9	0.963	0.361
	homocysteine (Cys), an amino acid	16.08±2.40	15.97±2.23	9	0.958	0.347

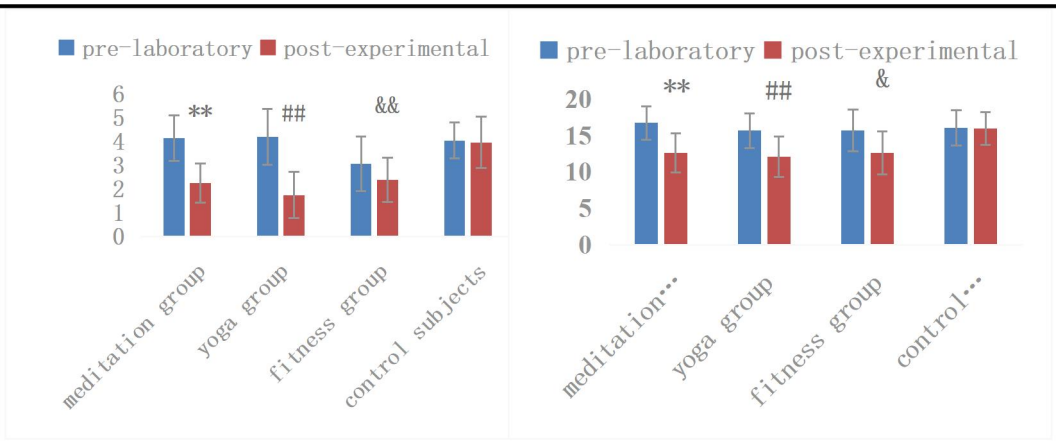


Figure 3: Within-group comparison of MDA and HCY before and after the experiment

*Expressing the pre- and post-exercise differences in the meditation group represents a significant difference *at* $P < 0.05$, ** indicates a highly significant difference *at* $P < 0.01$; # indicates the pre- and post-comparison in the yoga group, with a significant difference *at* $P < 0.05$, and ### indicates a highly significant difference at $P < 0.01$; & indicates the pre- and post-training comparisons in the physical fitness group, with a significant difference *at* $P < 0.05$, &&& amp;
indicates a highly significant difference *at* $P < 0.01$; Φ indicates a significant difference *at* $P < 0.05$ for pre- and post-exercise comparisons in the control group, and ΦΦ indicates $P < 0.01$.

2.2.2 Between-group comparisons of different exercise modalities on MDA and HCY in female drug users

Table 6: Between group comparison of different exercise modalities on MDA, HCY among female drug users

norm	meditation group	yoga group	fitness group	control subjects	P
MDA	2.26±0.82**@	1.76±0.98**@	2.40±0.93**#&	3.97±1.08#&@@	0.000
homocysteine (Cys), an amino acid	12.61±2.69**	12.08±2.75**	12.62±2.94**	15.97±2.23#&@@	0.000

Note: ** denotes a highly significant difference with P < 0.01 when compared to the control group; # denotes a significant difference with P < 0.05 when compared to the meditation group, ## denotes a highly significant difference with P < 0.01; & denotes a significant difference with P < 0.05 when compared to the yoga group, && denotes a highly significant difference; @ denotes a significant difference with P < 0.05 when compared to the physical fitness group, and @@ denotes a highly significant difference with P < 0.01. P < 0.05 has a significant difference and @@ indicates a highly significant difference with P < 0.01.

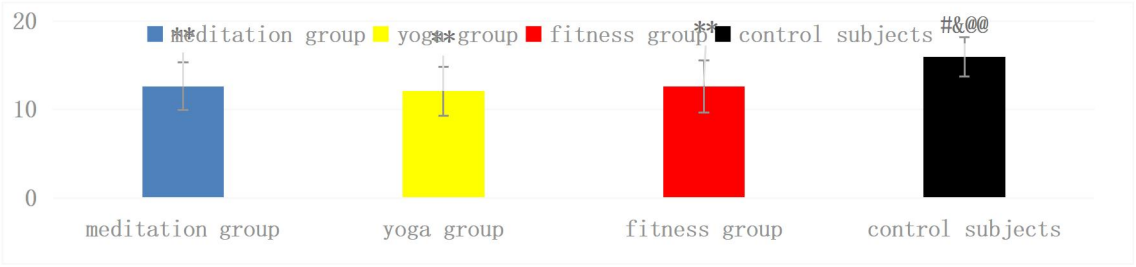


Figure 4: Comparison between groups of different exercise modalities on MDA, HCY of female drug users

2.3 Effect of different exercise modalities on blood inflammatory factor levels in female drug users

2.3.1 Within-group comparison of different exercise modalities on inflammatory factor levels in female drug users

Table 7: Within-group comparison of different exercise modalities on inflammatory factors in female drug users

groups	norm	pre-testing	post-test	(number of) degrees of freedom (physics)	T	P
contemplation	TNF-A	60.94±14.31	44.55±10.60*	9	-2.780	0.021
	IL-6	31.27±7.36	21.71±3.80**	9	2.861	0.019
	IL-1	73.32±15.61	44.84±12.60**	9	4.809	0.001
	ICAM-1	343.01±73.84	217.39±60.03**	9	3.510	0.007
yoga (loanword)	TNF-A	63.87±24.72	38.25±13.65#	9	2.729	0.023
	IL-6	32.87±9.27	23.26±6.59##	9	3.249	0.010
	IL-1	76.32±13.12	52.36±14.01##	9	3.249	0.010
	ICAM-1	317.30±85.34	189.96±70.64##	9	3.606	0.006
stamina	TNF-A	66.84±23.05	37.08±14.26&	9	3.985	0.023
	IL-6	29.92±5.74	17.11±5.83&	9	2.806	0.021
	IL-1	71.14±13.70	49.92±16.67&&	9	2.991	0.015
	ICAM-1	334.29±57.99	215.19±61.51&&&	9	0.795	0.000
control subjects	TNF-A	62.01±16.73	60.34±16.45	9	0.776	0.337
	IL-6	28.07±6.61	26.26±6.16	9	0.803	0.112
	IL-1	72.83±12.60	69.36±13.01	9	-1.129	0.289
	ICAM-1	343.01±73.84	334.29±57.99	9	0.724	0.488

Note: * denotes pre- and post-exercise differences in the meditation group, representing a significant difference *with* $P < 0.05$, ** denotes $P < 0.01$ with a highly significant difference; # denotes pre- and post-exercise comparisons in the yoga group, with a significant difference with $P < 0.05$, and ## denotes $P < 0.01$ with a highly significant difference; & denotes pre- and post-exercise comparisons in the physical group, with a significant difference with $P < 0.05$, &amp ;& denotes $P < 0.01$ with highly significant difference; Φ denotes pre- and post-exercise comparisons in the control group, $P < 0.05$ with significant difference, and ΦΦ denotes $P < 0.01$.

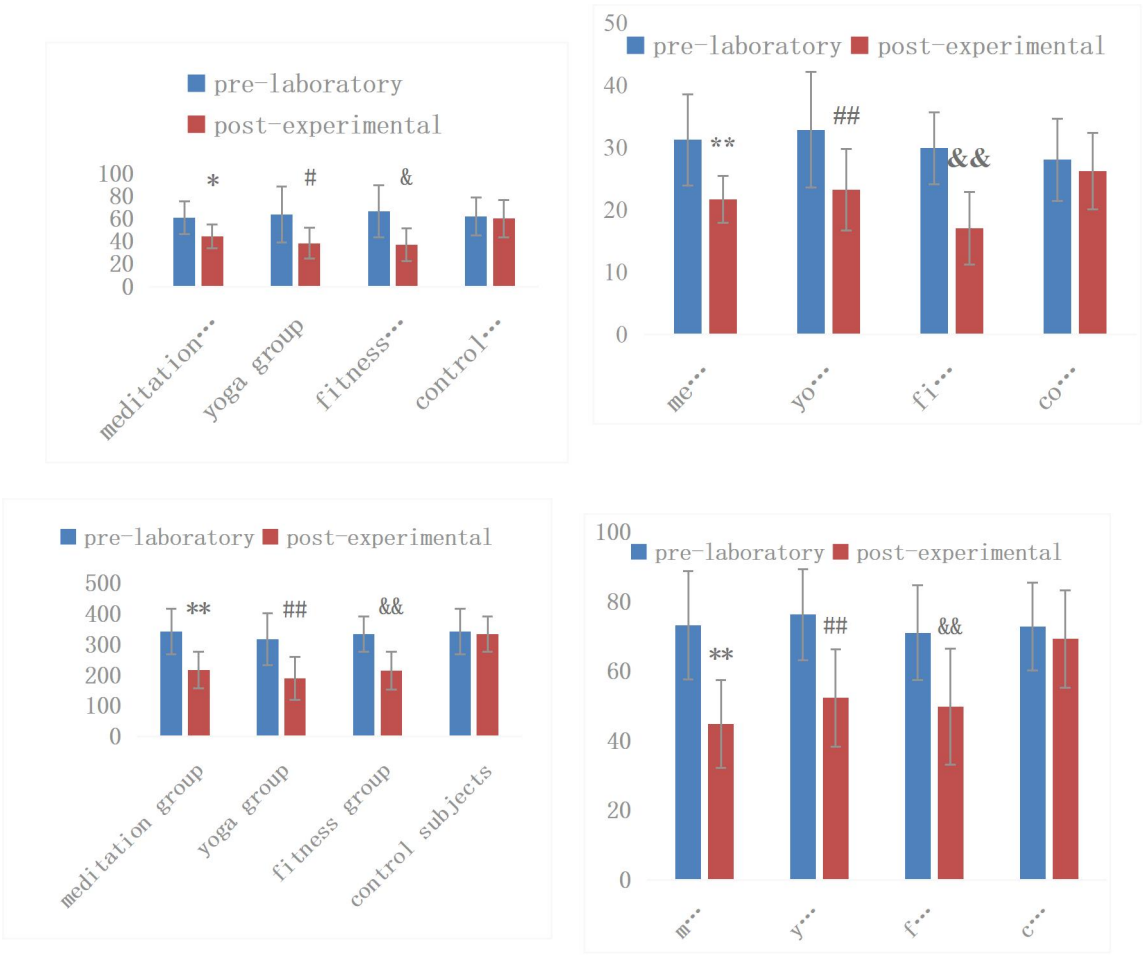


Figure 5: Comparison of different exercise modalities on TNF-A, IL-6, IL-1, ICAM-1 in female drug users

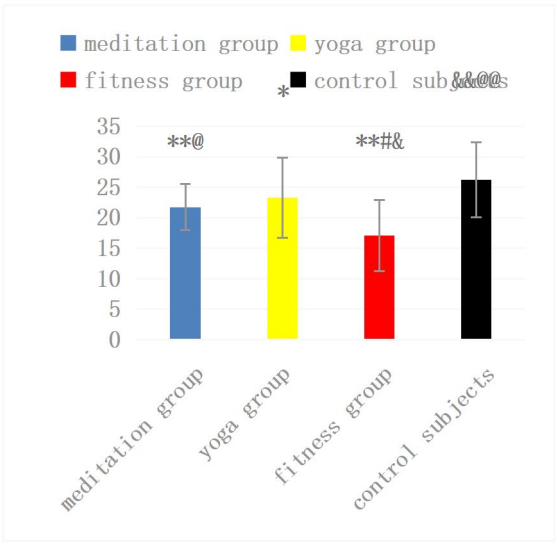
2.3.2. Between-group comparison of different exercise modalities on blood inflammatory factor levels in female drug users

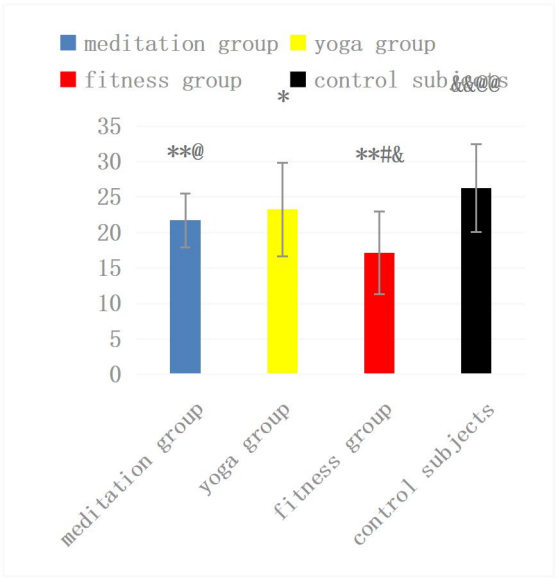
Table 8: Intergroup comparison of inflammatory factors in female drug users by different exercise modalities

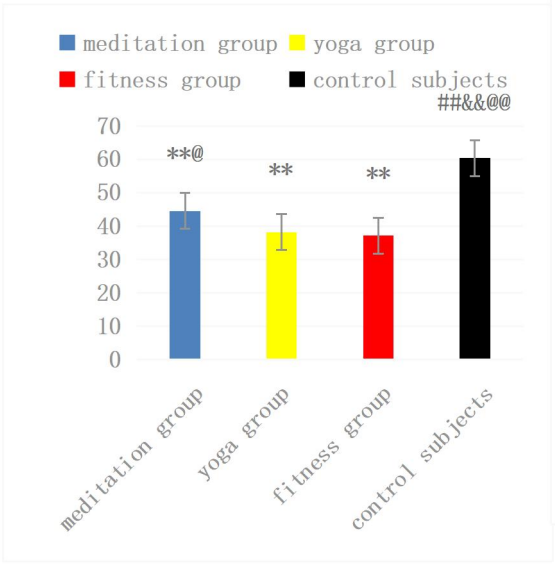
norm	meditation group	yoga group	fitness group	control subjects	P
TNF-a	44.55±10.60**@	38.25±13.65**	37.08±14.26**	60.34±16.45##&&@@	0.000
IL-6	21.71±3.80**@	23.26±6.59**@	17.11±5.83**#&	26.26±6.16&&@@	0.000
IL-1	44.84±12.60**&	52.36±14.01**#	49.92±16.67**	69.36±13.01##&&@@	0.000
ICAM-1	217.39 ± 60.03**&&	189.96±70.64**@@	215.19±61.51**&&	334.29±57.99##&&@@	0.000

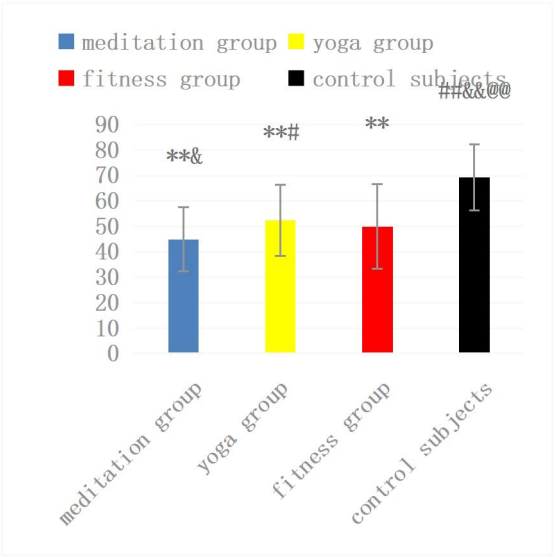
Note: ** denotes a highly significant difference with P < 0.01 when compared with the control group; # denotes a significant difference with P < 0.05 when compared with the meditation group, ## denotes a highly significant difference with P < 0.01; & denotes a significant difference with P < 0.05 when compared with the yoga group, && denotes a highly significant difference with P < 0.01; @ denotes a significant difference with the physical fitness group, P < 0.05 is a significant difference and @@ indicates a highly significant difference with P < 0.01.

Figure 6: Between-group comparison of different









exercise modalities on TNF-a, IL-6, IL-1, ICAM-1 levels in female drug users

2.4 Effects of different exercise modalities on VAS among female drug users

Table 9: Effect of different exercise modalities on VAS among female drug users

drug craving	groups	pre-testing	post-test	(number of) degrees of freedom (physics)	T	P
VAS	yoga group	7.20±1.68	5.0±1.82**	9	6.128	0.001
	meditation group	7.20±2.20	5.5±1.84**	9	4.019	0.003
	fitness group	7.10±1.66	5.3±2.16**	9	3.85	0.004
	control subjects	7.40±1.95	7.20±1.13	9	0.361	0.726

Note: The drug craving scale is based on the Visual Analogue Scale: VAS; * represents a significant difference of $P < 0.05$ when comparing the same group before and after the intervention; ** indicates a highly significant difference of $P < 0.01$.

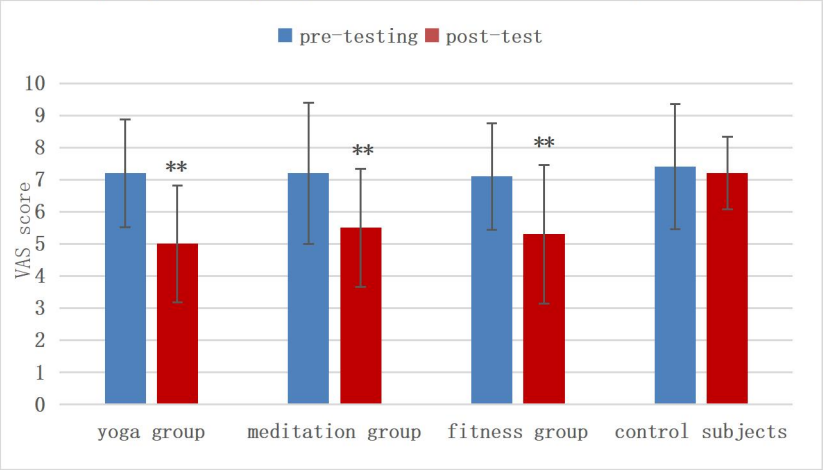


Figure 7: Change in drug craving in different groups before and after the trial

3. Analysis and discussion

3.1 The body of the drug user is in a state of oxidative stress and chronic inflammation during withdrawal

Neurological disorders are characterised by an inflammatory response in the body: e.g. autism, bipolar disorder, schizophrenia, Alzheimer's disease, etc.[39-42] . Drug use is also a chronic brain disease, and the interaction between drugs and the immune system leads to

neuroinflammation in the brains of drug users, a key mechanism in the development and maintenance of substance use disorders. Inflammatory changes affect dopamine and glutamate signalling within the brain, disrupting dopamine and glutamate transporter function as well as signalling pathways. Downregulation of dopamine, glutamate transporter proteins and increased relapse and drug craving behaviours in animals treated with cocaine [43, 44] .

The study of Wang Jingsong and Jiang Liang on the level of inflammation in the body of drug addicted patients found that: serum levels of pro-inflammatory IFN-Y and IL-9 were significantly higher than those of normal people, while anti-inflammatory factors IL-4, TGF-PL and IL-7 were significantly lower than those of normal people; Wan Fen's study also confirmed that: with the continuous increase in the duration of the use of methamphetamine and the dose of methamphetamine, the expression level of TNF-alpha, IL-6, and IL-1β significantly increased in the users' body; in addition, animal experiments also found that MDA use increased microglial cell activation to different degrees in different brain regions of addicts. -1β expression levels in users [33, 45, 46] , and microglial cells in different brain regions of addicts have different degrees of activation; in addition, animal experiments have also found that the use of MDA increases the expression of pro-inflammatory factors, such as TNF-α, IL-6, etc., in the brains of mice. **The results of the present study also indicate that female drug addicts are in a state of long-term high oxidative stress and chronic inflammation, which is manifested by elevated concentrations of MDA, HCY, ICAM-1, TNF-α, and IL-6, and may be associated with the maintenance of addiction and relapse behaviours.**

3.2 Aerobic exercise reduces the levels of oxidative stress and inflammatory factors in the bodies of drug users

Persistent chronic inflammation in the brain has been shown to be closely related to drug relapse and maintenance of drug craving state. Zhou Chenglin, Wang Dongshi et al. demonstrated that regular exercise can reduce oxidative stress and inflammation levels in drug addicts, enhance neuroplasticity in the brain, and effectively improve their depression, inhibitory control, and withdrawal syndromes.([32]) ; Lu Chunxia et al.'s intervention experiments showed that 12 weeks of aerobic combined with resistance training exercise can significantly reduce the IL-9 concentration in drug-dependent individuals, and can cause benign changes in the concentrations of IL-17, IL-9, and IL-19 cytokines, indicating that the inflammatory response is closely related to the maintenance of the drug craving state. -9 and IL-19 cytokine concentrations undergo benign changes, reducing the body's inflammatory

response, indicating that exercise not only reduces the level of pro-inflammatory cytokines, inhibits the activation of neuroglia and relieves neuroinflammation, but also effectively restores the permeability of the body's blood-brain barrier, which makes it difficult for peripheral inflammatory factors to enter the central nervous system, thus reducing neurotoxicity.([47, 48]) ; eight weeks of moderate exercise can improve the level of IL-9 concentration in morphine-dependent rats. Exercise can increase serum IFN-y and IL-6 levels in morphine-dependent rats and improve morphine withdrawal effects and physical function. Therefore, continuous moderate-intensity exercise and short-duration high-intensity exercise have significant effects on reducing the level of inflammation in the body of drug addicts [26, 29] . **The results of this study showed that the physical training group was able to reduce the concentration of MDA and HCY, improve the antioxidant capacity of the body, and reduce the expression of inflammatory factors IL-1, IL-6, ICAM-1, and TNF-α in female drug addicts. In conclusion, the levels of oxidative stress and chronic inflammation in female drug users were reduced, contributing to the formation of inflammatory homeostasis.**

3.3 Yoga reduces the level of oxidative stress and inflammatory factors in the bodies of drug users

Yoga as an effective alternative therapy in SUD (Substance Use Disorder) has been found to reduce stress and addictive behaviours while improving self-esteem and increasing self-control, relieving pain and anxiety-depressive states, especially in female drug users, the exact mechanism of action is unknown, yoga reduces addictive behaviours, enhances well-being and improves cognitive flexibility.

The possible mechanisms are that yoga is an aerobic exercise that effectively promotes self-regulation through distraction and increased stress coping, improves cognitive functioning (response inhibition) in drug users, improves mental health symptoms, sleep and quality of life, and can also have a significant impact in terms of blood pressure, lung capacity, flexibility, and aerobic endurance, improves self-control in women, and reduces substance use ([49-55]) .

Stopping drug intake increases inflammation levels in quitters and prolonged exposure to stress releases cortisol. Yoga reduces cortisol and ACTH (adrenocorticotropic hormone) levels in quitters, modulates central stress response and autonomic homeostasis, reduces inflammation and alleviates negative emotions, affects immune function in a beneficial way, and helps drug-dependent individuals to reduce drug cravings [56-58] . **The present study**

shows that yoga reduces oxidative stress and inflammation levels in the body, as evidenced by reduced levels of MDA and HCY, IL-6, ICAM-1, TNF-α.

3.4 Meditation reduces levels of oxidative stress and inflammatory factors in the bodies of drug users

In recent years, research on meditation as an important therapy has developed rapidly and has been widely used in clinical medicine. Meditation activates the limbic dopaminergic pathway in the midbrain, the same mechanism by which drug abuse acts on the brain, and in this sense meditation can be used as a substitute for the psychobiological functions previously performed by drug abuse. Meditation has a strong impact on brain structure and function, as well as on epigenetic and telomere regulation, and its applications have been progressively expanded to include emotional distress in substance-related and addictive disorders, craving and withdrawal symptoms, and neurological disorders such as schizophrenia. A meta-analysis of studies has demonstrated that meditation practice induces sustained structural changes in eight regions of the brain, improves brain functioning, establishes extensive network connectivity, enhances autonomic functioning, and modulates the expression of inflammatory cytokines in a variety of disorders. For example, MBSR (Massive Mindfulness-Based Stress Reduction Therapy) prevents the downregulation of interleukin (IL)-10 in patients with fibromyalgia; reduces the levels of IL-6 and TNF-alpha in patients with primary open-angle glaucoma, and helps to keep the inflammatory cytokines in the body in a finely-tuned balance, sometimes promoting inflammatory responses and sometimes inhibiting excessive inflammatory responses [59] .

Meditation reduces craving behaviours in drug users, relieves pain in patients with chronic pain comorbid with opioid addiction, and suppresses opioid cravings [60] The following mechanisms may be involved in the effects of meditation on drug addiction recovery: relieving stress by lowering cortisol; meditation training enhances ACC, PFD activity, and enhances connectivity of brain regions associated with self-control and emotion regulation; improving attention and self-regulation through interactions between the central nervous system and autonomic nervous system, and inducing neuroplasticity associated with drug addiction; adopting a non-judgmental stance to reduce drug-seeking behaviours caused by negative emotions, conflict, and stress, and improving emotion regulation to enhance self-control The interactions between the central and autonomic nervous systems improve attention and self-regulation and induce neuroplasticity associated with drug addiction; adopting a non-judgemental stance reduces drug-seeking behaviours caused by negative

emotions, conflicts and stress, and overcomes drug cravings by improving emotional regulation and enhancing self-control, leading to better treatment of addiction and prevention of relapse. **The present study showed that meditation reduced MDA, HCY, TNF-α, IL-6, IL-1, ICAM-1 levels in the blood of drug users**.

Current researchers have used different meditation methods and different training times, which has resulted in an inability to systematically assess which type of meditation is more beneficial for which populations or diseases and has not fully elucidated the biological mechanisms of meditation. In the future, further randomised controlled studies targeting selective meditation subtypes and prescribed training times with sufficient samples are needed to determine the efficacy of meditation, and to investigate the mechanisms of meditation on mind-body interactions, which can better demonstrate the positive role of meditation as an ancient mind-body therapy in promoting human health.

3.5 Physical fitness, yoga, and meditation all reduce drug cravings in drug users

The present study assessed the effects of three different exercise modalities on the drug craving levels of female drug addicts through VAS. For example, Wang Dongshi had conducted a 12-week randomised controlled trial on 63 drug-dependent persons, and the exercise group was required to undergo a moderate-intensity (65%-75% HRmax) aerobic exercise intervention three times a week for 30-40 min each time, and the subjects' drug craving was assessed using the VAS at baseline and after 3 weeks of exercise, and the results showed that: the craving level of the exercise group decreased significantly from the 6th week onwards and until the end of the exercise intervention [61] ;

A meta-analysis showed that drug craving improvement was significant in five studies, but drug craving levels did not improve after 4 weeks of participation in aerobic exercise in eight studies, and it was hypothesised that the possible reasons for this may be due to the level of drug craving being related to the exercise elements (mode of exercise, intensity, duration, frequency, etc.), an unstructured training programme, or a small sample size. **The 12 weeks of physical training in this experiment reduced drug craving scores in drug users.**

In recent years studies have found yoga to be more effective in reducing levels of craving for drugs and have demonstrated the potential clinical utility of yoga as an adjunctive withdrawal intervention [62] . Possible reasons for this may be due to the fact that yoga activates reward pathways associated with drug abuse, particularly the midbrain limbic

dopamine system, improving negative emotional states, while focusing on breathing exercises and concentrating on the breath may reduce the severity and frequency of the urge to use drugs again, and also that breathing can help addicts to relax, thus counteracting common withdrawal symptoms, as voluntary slow deep breathing inhibits sympathetic nerve activity, which may alleviate withdrawal symptoms. In addition, addictive drugs lead to hypoxia and hyperactivity in the respiratory-related insula, lesions in this region are associated with relapse, breathing exercises reduce drug cravings through effects on the insula cortex, and yoga can be used as a lifelong exercise programme and enhance withdrawal effects. **The present study concludes that yoga can be effective in the short term in reducing substance use, decreasing drug craving and preventing relapse, however more research is needed to prove the long term effects of yoga on drug addicts.**

In a randomised controlled trial to examine the relationship between meditation and drug relapse, subjects in both the meditation and control groups were followed up for 15 weeks, and the results of the study showed a significant reduction in the number of days of self-reported drug use in the meditation group compared to the control group.([63]) ; Bowen and his team found that subjects in the meditation group experienced a significant reduction in drug craving compared to the control group, which was reflected in significantly lower drug use and relapse rates. Subsequently, the team further revealed the underlying mechanisms, and the results showed that the conscious regulation of current attention and thoughts, as well as the non-judgemental acceptance of the emotional state and inner feelings at the time during meditation practice were effective in preventing and reducing the level of drug cravings during withdrawal [64, 65] . **Currently, meditation has been widely used in clinical medicine, but the application of meditation in the field of drug addiction has not yet formed a system, and the intrinsic mechanism between meditation and drug withdrawal needs to be further explored. The present experiment demonstrated that drug craving scores could be reduced by a 12-week meditation intervention.**

In conclusion: all three modes of exercise can reduce oxidative stress and body inflammation levels and drug craving in drug abusers. Yoga and meditation, although acting on the body with smaller loads, can achieve the same inflammation-reducing effect as physical training with larger loads, and are more acceptable and implementable for weaker drug abusers, so that yoga and meditation, with their smaller loads, can be promoted to all stages of drug treatment, even the acute phase; or Combined with aerobic exercise, the flexible use of mixed interventions is more conducive to corrective

effects, and more human experiments are needed for research in this area, and its mechanisms require further study.

4 Conclusion

4.1 There are oxidative stress and inflammatory reactions in the body of female drug addicts during the audit period, which are manifested in increased concentrations of MDA, HCY, TNF-α, IL-1, IL-6 and ICAM-1 in the serum weight.

4.2 Aerobic physical fitness, yoga and meditation can all improve the level of oxidative stress and inflammation in the bodies of drug users.

4.3. Aerobic fitness, yoga, and meditation all improve drug craving among drug users as well as drug abusers

4.4 There is a correlation between oxidative stress inflammatory factors and drug craving in the bodies of drug abusers, and exercise reduces drug craving by lowering the body's inflammatory response.

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