Effect of Eight-Month Exercise Intervention on Bone Outcomes of Young Opioid-Dependent Women

Yubing Xu
Institute of Intelligent Machines Chinese Academy of Sciences
Zenghui Ding (dingzenghui@iim.ac.cn)
Chinese Academy of Medical Sciences & Peking Union Medical College Hospital of Skin Diseases and Institute of Dermatology https://orcid.org/0000-0002-6787-9318
Yanyan Chen
Institute of Intelligent Machines Chinese Academy of Sciences
Mu Wang
Institute of Intelligent Machines Chinese Academy of Sciences
Zijun He
Institute of Intelligent Machines Chinese Academy of Sciences
Yuan Wang
Institute of Intelligent Machines Chinese Academy of Sciences
Yining Sun
Institute of Intelligent Machines Chinese Academy of Sciences
Huazhi Li
Women's Specific Drug Rehabilitation Center of Anhui Province
Zuchang Ma
Institute of Intelligent Machines Chinese Academy of Sciences

Research article

Keywords: Drug Abuse, Exercise Intervention, Bone quality, Body Composition

Posted Date: June 29th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-35260/v1

Abstract

Background: The purpose of this study was to evaluate bone response to an 8-month aerobic gymnastics training program in young opioid addicted women.

Method: One hundred and two young women with previous opioid addiction were divided into two groups: (a) low bone quality intervention experimental group (n=55); (b) low bone quality observed control group (observation group) (n=47). Intervention group took aerobic gymnastics regularly for 120 $min \cdot d^{-1}$, $5d \cdot wk^{-1}$ for 8 months and completed follow-up testing. Substance use history and other life habit affecting bone quality were assessed by questionnaire-based interviews. Bone quality (stiffness-index, T-score, Z-score) was examined with quantitative ultrasound. Anthropometric characteristics (body weight, fat free mass, fat mass) were obtained by bioelectrical impedance analysis.

Results: After 8-month intervention, the stiffness-index of bone quality increased significantly (before: 82±6, after: 108±14, $p<0.05$) in the experimental groups. However, the bone quality did not change significantly in the controls (observation group: before: 79±10, after: 77±13, $p>0.05$). Fat mass decreased in experimental group (Experimental group: before: 19.6±3.7kg, after: 18.8±4.0kg, $p<0.05$). Meanwhile, change of fat-free mass was the determination of change of bone quality in the experimental group.

Conclusions: Our results suggested that aerobic gymnastics intervention can be an effective strategy for the prevention and treatment of drug-induced osteoporosis in detoxification addicts.

1. Background

Long-term opioid dependence in young person will lead to drug-induced osteoporosis. Those drugs will affects bone metabolism and reduced trabecular bone mass, or suppress hypothalamic secretion of gonadotropin-releasing hormone and consequently decreases the level of gonadal hormones and lead to low bone quality and later-life osteoporosis (Ding et al., 2017; Gotthardt et al., 2016). Osteoporosis is an age-related disease, characterized by a progressive loss of bone quality and micro-architectural deterioration, predisposing to fracture after minimal trauma or fall (Harvey et al., 2014). Although osteoporosis is typically thought to develop as a result of normal age-related losses in bone, persons who fail to attain their maximum peak bone mass during critical growing years may increase their risk of having osteoporosis (Nordström et al., 2013). Kay et al. reported that substance abuse in women yielded a higher risk of a variety of health problems than substance abuse in men (Kay et al., 2010). Drug intervention is considered to be the primary method of recovery of the musculoskeletal system, but its long-term safety is uncertain (Khan et al., 2017).

Exercise intervention could be an important means of prevention and treatment of drug-induced osteoporosis. Exercise for optimizing peak bone mass in young women will beneficial for their elder life (Bailey, C.A. 2008). Bone is inherently mechanosensitive, responding and adapting to its mechanical environment (Mellon and Tanner, 2012). Regular exercise has effects on bone density, size, and shape, resulting in substantial improvements in mechanical strength (Tveit et al., 2015). It’s well known that high-impact can enhance bone health in premenopausal women (Carter and Hinton, 2014), but high-intensity exercise will bring more exercise risks to the sick people, treatment options should be appropriate to their specific situation (Senderovich et al., 2018). Aerobic exercise was also reported to have benefit to bone health by significantly reduced bone resorption activity (Ayudthaya and Kritpet, 2015; Wen et al., 2016). Few studies had focused on the effects of aerobic training on bone quality, fat-free mass (FFM) and fat mass (FM) of young opioid addicted women. These questions merit further investigation.

In addition, body composition had been reported to be an important determination of bone quality (Ding et al., 2016). Many reports FFM had positive relationship with bone quality (Bakker et al., 2003; Wang et al., 2005). However, it's uncertain that if the changes of FFM was the determinant of changes of bone quality. We had put forward a research hypothesis that increasing the degree of FFM through special physical training program could be a treatment for improving the bone health of women with drug addiction in our previous study (Ding et al., 2017).

Within a cohort of young opioid dependent women, the aim of our study was to evaluate the effect of an 8-month aerobic gymnastics training program on bone quality and body composition in young opioid dependent women, so that the suitable and effective non-pharmacotherapy intervention strategies could be employed to improve the bone health of young opioid addicted women.

2. Methods

2.1. Design, participants, recruitment and training process.

This was a longitudinal study of long-term opioid dependent women living in the middle area of China. Two hundred subjects were recruited from Women's Specific Drug Rehabilitation Center of Anhui Province between November 2015 and January 2018. Recruitment criteria were: 1) previous drug consumption of > 3 years, 2) newcomers (within 4 months), 3) age 20–40 years. They participated in a two-year isolation detoxification.

These participants would take medical examination and the questionnaire-based interviews, the exclusion criteria reduced the number of potential participants to 146. Exclusion criteria were: 1) significantly impaired renal or hepatic function, or chronic kidney disease; 2) Individuals with history of fractures in previous 24 months; 3) type 1 diabetes; 4) HIV infection; 5) pregnancy, because of the altered hormonal household (Ding et al., 2017). Patients refusing to follow-up in our study or who had withdrawn consent were also excluded. Finally, according to the conducting power calculation, a total of 113 patients aged 20–40 years were recruited (Ding et al., 2017).

Before the training program, all participants had the measurements of anthropometric characteristics and bone quality. Then, the samples were randomly divided in a double-blind experiment into two groups: (a) low bone quality intervention experimental group (osteopenia or osteoporosis) (T-score<-1; n = 62); (b) low bone quality observed control group (observation group) (T-score<-1; n = 51). We divided samples into two groups to assess the sensitivity of the population to aerobic intervention. Patients in experimental group would take 8-month aerobic gymnastics training from March 5, 2017 to November 5, 2017 and had body composition measurements and bone quality measurements at last. The patients in observation group didn’t take part in the exercise intervention, but they took part in all the body composition measurements and bone quality measurements. The nutrient intake during the training period of two groups was investigated and managed by nutrition experts. These nutrition experts surveyed the diet of two groups through questionnaires every week and given dietary guidance, so that the calcium intake of the two groups was adequate and at the same level. Finally, one hundred and two patients (experimental group: n = 55, and observation group: n = 47) attended all the experimental process, eleven people lost to follow-up due to joint problems or other problem.

The research was approved by Research Ethics Committee of Hefei Institutes of Physical Science, Chinese academy of sciences. All participants provided informed consent, and the study was conducted in accordance with the guidelines in Institute and Intelligent of Machines, Chinese Academy of Science.

2.2. Questionnaires - background characteristics

The questionnaires-based interviews were designed to get comprehensive information about all the participants. The questionnaires included four parts: medical history, history of drug use, smoking history, nutritional calcium intake, as shown in Table 1.

Table 1
Questionnaires to the low bone quality intervention experimental group and low bone quality observation control group

Questions	Data Type
Medical history:	
1. Individuals with history of fractures in previous 24 months	0 = No 1 = Yes
2. Pregnancy	0 = No 1 = Yes
3. Type 1 diabetes	0 = No 1 = Yes
4.Significantly impaired renal or hepatic function, or chronic kidney disease	0 = No 1 = Yes
History of drug use (Patients only):	
1.Type of drug use: (1) Heroin, opium, morphine, and other opiates (2) Cocaine (3) Marijuana (4) Amphetamines (5) Hallucinogens (6) Other drugs	Multi selection
2. Age at onset of drug intake (year)	Quantitative
3. Duration of drug intake (years)	Quantitative
4. Frequency of drug use: (1) 3–7/week or more (3) 1–2/week (4) 1–2/month (5) seldom	Single selection
5. Way of drug use: (1) injection (2) non injection	Single selection
6. Duration of methadone intake (weeks)	Quantitative
7. Daily methadone dose (mg)	Quantitative
8. Duration of drug intake (years)	Quantitative
Smoking history:	
(1) often (2) occasionally (3) seldom	Single selection
Nutritional calcium intake during the training period:	
1.Diet: (1) well-balanced diet, regular intake of calcium-rich foods (2) Occasionally intake of calcium-rich foods (3) Low nutritional calcium intake, seldom intake of calcium-rich foods	Single selection

To make sure the accuracy of survey results, comparisons were made between patients' answers and medical examination and the official data, and the discrepancy would be confirmed by the individuals again.

2.3. Measurements of anthropometric characteristics

Body height (BH) was measured to the nearest 0.1 cm using a stadiometer (GMCS-I, XinDongHuaTeng Corp., China). Body weight, FFM, and fat mass (FM) were measured by bioelectrical impedance analyzer (BX-BCA-100, Broshare Technology Corp., Hefei, China) (Ding et al., 2017), and the REG. NO. in the China Food and Drug Administration (CFDA) is 2210038. In order to eliminate the effects of diuretics, alcohol, intense exercise and fluids on the measurement, subjects emptied their bladder 30 min before the bioelectric impedance analyses (BIA) measurement. Subjects stood on bare feet with the heel and toe of each foot in contact with the metal footpads, with arms lightly holding the two analyzer handgrips (Ding et al., 2017). Coefficient of variance (CV) of the impedance measure was 0.4%. Values obtained from BIA were supported by skinfold measurement using harpenden calipers (Ding et al., 2017).

2.4. Measurements of bone quality

Bone quality was measured by a quantitative ultrasound (QUS) device (BX-BDI-500A, Broshare Technology Corp., Hefei, China), which had been verified by clinical experiments with the REG. NO. of 20152230048 in CFDA. Speed of sound (SOS; m/s) and broadband ultrasound attenuation (BUA; dB/MHz) were measured on the right calcaneus. The stiffness-index (SI), which has a lower precision error than either SOS or BUA alone, is calculated by the system according to the following formula: $SI = 0.67 \times BUA + 0.28 \times SOS - 420$ (Njeh et al., 1997). SI provided information of bone structural parameters besides BMD, and higher SI value indicates better bone health. SOS, BUA and SI have become common indexes to assess bone health (Lejla et al., 2018). Besides, values were also calculate as T-score and Z-score, which was generated based on SI in QUS device (Liu et al., 2012).

Bone quality of all the participants was diagnosis as normal (T-score >= -1.0), osteopenia (-2.5 < = T-score < -1.0), or osteoporosis (T-score < -2.5). The measurement took 5 min for each subject. To make sure of the precision of QUS measurements, each of 10 subjects aged between 20 and 40 years received 20 measurements before every measurement. The values for SOS, BUA and SI varied in the range 1489–1623 m/s, 42–133 dB/MHz and 62–130, respectively, and the respective standard deviations were between 4 and 11 m/s, 1 and 5 dB/MHz and 1 and 4. The calculated coefficients of variation were 0.4%, 2.0% and 2.5% for SOS, BUA and SI, respectively.

2.5. Aerobic gymnastics protocol

Two days after the initial 60-min trial, Experimental group began training 2 times (Morning: 60-min, Afternoon: 60-min) 5 days per week, completing an 8-months aerobic gymnastics exercise training program. The exercise training consisted of stretching and warm-up exercises (10–15 min), dynamic aerobic activities (35–40 min) involving stepping, skipping, graded walking, hopping, jogging, jumping, dancing, step choreographies, and cool-down/relaxation exercises (10 min). All sessions were accompanied by appropriate music relevant to the required activity. The intensity of exercise was investigated by the rate of perceived exertion (RPE) of the Borg scale after every day's training program (Borg, 1985), and the training program was guided and corrected by the coach, so that the intensity involved 40–60% of an individual's maximal capacity, a level at which physical health benefits can be obtained. Meanwhile, the dynamic aerobic activities, as the core exercise intervention, should last for 35–

40 min, so that body circulatory system can be fully mobilized. The observation group didn't take part in any training programs. The physical activity level of observation group was regularly investigated by questionnaire. Meanwhile, the observation group was available for all the examination.

2.6. Statistical analysis

Age, anthropometric characteristics, SI and T-score were expressed as mean ± standard deviation. P value less than 0.05 was set as level of significance. Student's t-test was done for comparison of means and quantitative data between low bone quality intervention experimental group and low bone quality control group. P values, two-tailed, < 0.05 were considered statistically significant. Paired t-test was used in comparing values before and after experiment. Independent t-test was used in comparing between experimental group and control group. The association of the change of SI ($\varDelta\mathrm{SI}$) with each of the relevant factors (age, smoking status, body weight, FFM, FM, rate of fat mass (%Fat mass), SI, change of body weight ($\varDelta$Body weight), change of fat-free mass ($\varDelta$Fat-free mass), change of fat mass ($\varDelta$Fat mass)) was explored using linear regression. In a step further, relationships between the outcomes and factors of interest and potential determinants, including body weight, FFM, FM, %Fat mass, SI, $\varDelta$Body weight, $\varDelta$Fat-free mass, $\varDelta$Fat mass were investigated using multivariable linear regression. All statistical analyses were conducted using SPSS for Windows, Version 22.0 (IBM Corp., Armonk, NY).

3. Results

3.1. Baseline characteristics of participants

As listed in Table 2, experimental group and observation group did not differ with regard to age, BH, BW, BMI, FFM, FM and the bone quality (SI and T-Score). What else, there was no difference in the type of drug use and way of drug use in the two groups. Meanwhile, in the course of experiment, most of the samples in the two groups had well-balanced diet and regular intake of calcium-rich foods.

Table 2
Baseline characteristics of the low bone quality intervention experimental group and low bone quality observation control group

Variable	**experiment group** (n = 55)	**observation group** (n = 47)	***P***
Age(years)	30.3 ± 6.1	29.0 ± 5.3	0.332
Anthropometrics			
Body height (cm)	162 ± 4.9	162 ± 5.1	0.726
Body weight (kg)	62.7 ± 6.8	62.6 ± 6.4	0.993
Body mass index (kg/m^2)	24.1 ± 2.4	24.0 ± 2.4	0.520
Fat Free mass (kg)	44.0 ± 2.9	42.5 ± 3.1	0.126
Fat mass (kg)	19.6 ± 3.7	20.0 ± 4.4	0.840
Drug history			
Heroin, opium, morphine, and other opiates (% of n)	87%	86%	0.482
Cocaine and other drugs (% of n)	73%	66%	0.115
Multi substances (% of n)	53%	61%	0.183
High frequency of drug use [a]	88%	89%	0.365
Age at onset of drug intake (year)	21.7 ± 5.4	21.5 ± 4.4	0.578
Injecting drug users (% of n)	17%	19%	0.135
Duration of drug intake (years)	8.6 ± 3.7	8.9 ± 3.1	0.563
Smoking (% of n)	96%	94%	0.854
Bone quality			
SI [b]	82 ± 6	79 ± 12	0.096
T-Score	-1.3 ± 0.3	-1.4 ± 0.8	0.121
Nutrient intake status during the training period			

The data are shown as mean ± standard deviation; ** Significantly different from the experiment group, $p < 0.05$.
a) High frequency of drug use: 3–7/week or more;
b) SI indicates stiffness index, SI = 0.67 × BUA + 0.28 × SOS−420.

Variable	experiment group (n = 55)	observation group (n = 47)	*P*
Well-balanced diet, regular intake of calcium-rich foods. (% of n)	93.6%	95.2%	0.256
Physical activity per day			
Aerobic gymnastics time (min)	120	——	——
The data are shown as mean ± standard deviation; ** Significantly different from the experiment group, $p < 0.05$.			
a) High frequency of drug use: 3–7/week or more;			
b) SI indicates stiffness index, $SI = 0.67 \times BUA + 0.28 \times SOS - 420$.			

3.2. Changes in anthropometrics

There was significant change in body composition in response to exercise intervention (Table 3). Body weight and FM significantly decreased in the experimental group ($P < 0.05$; $P < 0.05$, respectively). Meanwhile, there were significantly decreased occurred for BMI, Fat mass Index (FMI) and %FM only in the experimental group. However, no significant changes in FFM and FFMI were observed in the observation group (Table 3).

Table 3
Changes in anthropometric and bone quality

Characteristic	Experiment group (n = 55)	observed control group (n = 47)
	Before after	Before After
Anthropometrics		
Body weight (kg)	62.7 ± 6.8 60.9 ± 6.5*†	62.6 ± 6.4 62.5 ± 6.1
Fat-free mass (kg)	42.0 ± 2.9 42.2 ± 3.2	42.5 ± 3.1 42.9 ± 3.2
Fat mass (kg)	19.6 ± 3.7 18.8 ± 4.0*†	20.0 ± 4.4 19.8 ± 4.3
BMI (kg/m^2)	24.1 ± 2.4 23.4 ± 2.3*	24.0 ± 2.4 23.9 ± 2.3
FFMI (kg/m^2)	16.9 ± 1.5 16.1 ± 0.7	16.3 ± 0.7 16.5 ± 0.7
FMI (kg/m^2)	7.5 ± 1.4 7.2 ± 1.5*†	7.7 ± 1.8 7.4 ± 1.7
%FM	31.6 ± 6.3 29.7 ± 3.7*	31.7 ± 4.4 30.8 ± 4.5
Bone quality		
SI	82 ± 6 108 ± 14*†	79 ± 10 77 ± 13
T-Score	-1.3 ± 0.3 0.2 ± 0.7*†	-1.4 ± 0.5 -1.5 ± 0.7
Z-Score	-1.3 ± 0.4 0.4 ± 0.9*†	-1.5 ± 0.5 -1.5 ± 0.8

The data are shown as mean ± standard deviation;

* Significantly different from the same group before and after the experiment, $p < 0.05$;

† Significantly different from the changes between experiment and observed control group, $p < 0.05$;

FFMI indicates Fat-free mass index, Fat-free mass /height squared; FMI indicates Fat mass Index, Fat mass/height squared; SI indicates stiffness index, SI = 0.67 × BUA + 0.28 × SOS−420.

3.3. Changes in bone quality

After 8-month exercise intervention, there was significant effects occurred for SI (82 ± 6 VS 108 ± 14, $P < 0.05$) and Z-score (-1.2 ± 0.4 VS 0.4 ± 0.9, $P < 0.05$) in experimental group (Table 3), and the percentage of people who had an increasing bone quality was 100% (n = 55/55). The bone quality of experimental group was significantly increased by 32.8% at the calcaneus (Table 3). However, no significant changes in SI were observed for the observation group (Table 3).

Table 4 shows the multivariate regression analysis for the prediction of bone quality in the experimental group. Relationships between the changes of calcaneal bone stiffness-index ($\Delta \mathrm{SI}$) and factors of potential determinants (including body weight, FFM, FM, %Fat mass, SI, ΔBody weight, ΔFat-free mass, ΔFat mass) were investigated using multivariable linear regression. FFM and ΔFFM were the positive predictor for SI (P = 0.010;P = 0.004, respectively), while SI and ΔBody weight were the negative predictor for ΔSI (P = 0.016，P = 0.020, respectively).

Table 4
Multivariate regression analysis of changes of calcaneal bone quality in the low bone quality intervention experimental group.

Dependent variable	Independent Variable	Standard β	p
		Low bone quality intervention experimental group	
ΔSI [a]			
Model	Body weight	-4.390	0.077
	Fat-free mass	5.275	0.010
	Fat mass	0.765	0.562
	%Fat mass	0.103	0.936
	SI [b]	-0.126	0.016
	ΔBody weight [c]	-0.992	0.020
	ΔFat-free mass [d]	2.446	0.004
	ΔFat mass [e]	0.800	0.314
	$R^{=}$0.744		

a) ΔSI indicates changes of calcaneal bone stiffness-index;

b) SI indicates stiffness index before training program, SI = 0.67 × BUA + 0.28 × SOS−420;

c) ΔBody weight indicates changes of body weight;

d) ΔFat-free mass indicates changes of fat-free mass;

e) ΔFat mass indicates changes of fat mass.

Discussion:

3.4. Main findings

After 8-month exercise interventions towards the young opioid dependent women, we found that calcaneal bone quality was significantly increased and fat mass was significantly decreased in the experimental group, which was not found in the controls. As we know, age is an important determinant of bone mass, but the peak bone mass growth is mainly before the age of 20, and after the age of 20, especially after the age of 25, the bone mass growth is not significant (Weaver et al., 2016). Through the design of the control groups, we demonstrated the changes of bone and fat mass in the experimental group were not a natural recovery process. This study is novel because it is the first to demonstrate the efficacy of exercise-based interventions to increase bone quality in young opioid women with low bone quality.

Data on the effect of exercise interventions on bone quality of young opioid dependent women are limited. We only found some cross-sectional studies had reported that the effective physical activities were significantly lower in the illicit drug abuse women than the health controls (Ding et al., 2017; Milos et al., 2011). Furthermore, the reports on the effect of aerobics interventions in young healthy women were controversial. Heinonen et al. found that no significant changes in BMD were found in growing girl after 9 months of step aerobics (Heinonen et al., 2000). In contrast, Friedlander et al. reported that 2-year period, a combined regimen of aerobics and weight training has beneficial effects on BMD and fitness parameters in young women (Friedlander et al., 1995). Wen et al. reported that 10-week group-based step aerobics benefited to bone metabolism and general health by significantly reduced bone resorption activity and improved functional fitness in women with low bone mass (Wen et al., 2017). Our results further demonstrated this point of view in young opioid dependent women with low bone quality.

Compared with bone quality changes in the young opioid dependent women of experimental group, there was no significantly changes in the observation group. These differences may be due to the bone modeling and remodeling mechanisms to the mechanical stress. Frost first described the mechanisms of “minimum effective strain”(MES), which predicts the time and the site of bone architecture changes, as a result of adaptation to mechanical loads (Frost, 1987). Strains below the MES are not considered to produce adaptive bone modeling, whereas those above it change bone architecture, in order to reduce subsequent strains under loads (Frost, 1987; Frost, 2003). In our study, the experimental group took part in 8-months aerobic gymnastics exercise training program including the stepping, skipping, graded walking, hopping, jogging, jumping, dancing and step choreographies exercises. These exercises may promote bone quality through its direct mechanical loading effects on bone, and the mechanical stress on bone would activate osteoblasts and increase bone formation (Ehrlich and Lanyon, 2002). People in the observation group didn’t take part in any training program, therefore the mechanical load on the bone did not change, and the bone metabolism will not be activated (Rodan, 1997). We suggested that the changes of bone in the exercise intervention group were not a natural recovery process (Gleeson et al., 1990), but a result of adaptation to mechanical loads.

In addition, some have attempted to determine at what duration and frequency of loading is most responsive to the benefits of skeleton. Tsuji et al. reported that 3-month aerobic exercise had no effect on the bone quality, and they pointed that the 3-month period may have been insufficient to stimulate osteogenesis (Tsuji et al., 1996). The process of bone remodeling includes bone resorption and bone formation, and it needs sufficient time to complete the process (Tsuji et al., 1996). Some studies have confirmed that exercise intervention for six months can improve bone quality (Bailey, C.A. 2008). In our study, considering the particularity of the research sample, the training period was set as 8 months. High-frequency/high-cycle number exercise programs with low-to-moderate strain intensity were reported to have positively effect on bone strength of frail elderly (Kemmler and Von, 2011). We confirmed high-frequency/high-cycle number exercise programs with low-to-moderate strain intensity for 8 months were beneficial to bone health of young opioid dependent women with low bone quality.

We also found that 8-month aerobic gymnastics training program can be an effective strategy for the treatment of obesity in young opioid addicted under rehabilitation. After drug withdrawal, drug addicts will offset their dependence on drugs by consuming large amounts of food. Exercise intervention can be a healthy solution. Meanwhile, body composition is an important determinant of bone quality in general populations (Felson et al., 1993). In our study, our results further demonstrated that the changes of FFM was the determination of changes of bone quality in low bone quality intervention experimental group (Table 4), which was seldom reported in recent articles. Higher FFM lead to greater mechanical load on bone that results a better bone quality (Ehrlich and Lanyon, 2002; Rodan, 1997). Meanwhile, as an important component of FFM, muscle contractions can produce mechanical stress, and the mechanical stress on bone would activate osteoblasts and increase bone formation (Schiessl et al., 1998).

3.5. Implications for the treatment of opioid dependence

The findings of our study are of importance because it could be helpful for rehabilitation centers offering treatment programs. Aerobic training had been found to be a potential treatment for drug addiction, which may be related to its ability to facilitate dopaminergic transmission (Lynch et al., 2013; Smith et al., 2008), We further demonstrated that aerobic training were beneficial to the recovery of the bone quality of the young opioid addicted women. Increasing physician awareness of the exercise intervention effect on recovery of the bone quality of young opioid addicted women will allow for non-pharmaceutical interventions to prevent or treat drug-induced osteoporosis and other problems.

3.6. Strengths and Limitations

The strengths of our study are that similar studies focusing on the effect of exercise intervention to young opioid dependent women are scarce. Moreover, the experiment group and control groups were isolated in detoxification centers and participated in detoxification for two years, they had very similar living conditions and lived in the same macro environment, and the training programs were well executed. However, our results should be interpreted in light of several limitations. Firstly, other issues such as serum concentrations of total testosterone, vitamin D level, prolactin level, luteinizing hormone (LH) and sex hormone-binding globulin (SHBG) were not measured, Secondly, we did not include measurements of bone status at other sites or use additional techniques such as DXA. However, QUS measurement has become an important modality for the assessment of osteoporosis status (Liu et al., 2012;).

3.7. Conclusions

In conclusion, our study indicated the positive effect of 8-month aerobics exercise intervention for recovery of bone quality in young opioid dependent women. However, further research is needed to confirm these findings and to investigate whether such approaches could also be used in elders.

Abbreviations

BMI: Body Mass Index; FFM: Fat-free mass; FM: Fat Mass; QUS: quantitative ultrasound; BMD: bone mineral density; SOS: Speed of sound (m/s); BUA : broadband ultrasound attenuation (dB/MHz); SI: Bone stiffness-index.

Declarations

Ethics approval and consent to participate

The study was approved by the Research Ethics Committee of Hefei Institutes of Physical Science, Chinese academy of sciences. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

Yubing Xu, Zenghui Ding, Yanyan Chen, Mu Wang, Zijun He, Yuan Wang, Yining Sun, Huazhi Li and Zuchang Ma declare no competing interests.

Funding

This work was supported by the National Natural Science Foundation of China (No. 61701482 and No. 61603371), Natural Science Foundation of Anhui Province, China (No. 1808085MF191).

Author Contributions

ZHD led on all aspects of the study and paper writing. YBX and ZCM led on the statistical analyses and manuscript revise. ZJH & MW contributed to data collection. HZL played a key role in service user engagement. YYC & YNS wrote sections of the paper, with input from YW. All authors contributed to the design of the study and approved the final draft of the manuscript.

Conflict of Interest

Yubing Xu,, Zenghui Ding, Yanyan Chen, Mu Wang, Zijun He, Yuan Wang, Yining Sun, Huazhi Li and Zuchang Ma declare no competing interests.

References

1. Ayudthaya, W.C.N., Kritpet, T., 2015. Effects of Low Impact Aerobic Dance and Fitball Training on Bone Resorption and Health-Related Physical Fitness in Thai Working Women. Journal of the Medical Association of Thailand 98, S52-S57.
2. Bailey, C.A. , K. Brooke-Wavell . 2008. Exercise for optimising peak bone mass in women. Proceedings of the Nutrition Society 67, 9-18.
3. Bakker, I., Twisk, J.W.R., van Mechelen, W., Kemper, H.C.G., 2003. Fat-free body mass is the most important body composition determinant of 10-yr longitudinal development of lumbar bone in adult men and women. J Clin Endocrinol Metab 88, 2607-2613.
4. Borg GAV., 1985. An introduction to Borg's RPE-scale. New York: Mouvement Publications.
5. Carter, M.I., Hinton, P.S., 2014. Physical activity and bone health. Missouri medicine 111, 59-64.
6. Ding, Z., Chen, Y., Wang, X., Zhou, X., Xu, Y., Ma, Z., Sun, Y., Jiang, M., 2017. A comparison of bone quality and its determinants in young opioid-dependent women with healthy control group. Drug & Alcohol Dependence 175, 232.
7. Ding, Z., Chen, Y., Yang, X., Xu, Z., Xu, Y., Ma, Z., Sun, Y., 2018. Impact of Age, Gender, and Body Composition on Bone Quality in an Adult Population From the Middle Areas of China. J Clin Densitom 1,83-90.
8. Ehrlich, P.J., Lanyon, L.E., 2002. Mechanical strain and bone cell function: A review. Osteoporosis Int 13, 688-700.
9. Felson, D.T., Zhang, Y.Q., Hannan, M.T., Anderson, J.J., 1993. EFFECTS OF WEIGHT AND BODY-MASS INDEX ON BONE-MINERAL DENSITY IN MEN AND WOMEN - THE FRAMINGHAM-STUDY. J Bone Miner Res 8, 567-573.
10. Friedlander, A.L., Genant, H.K., Sadowsky, S., Byl, N.N., Glüer, C.C., 1995. A two-year program of aerobics and weight training enhances bone mineral density of young women. Journal of Bone &

Mineral Research the Official Journal of the American Society for Bone & Mineral Research 10, 574-585.

11. Frost, H.M., 1987. Bone "mass" and the "mechanostat". A Proposal Anat Rec 219, 1-9.
12. Frost, H.M., 2003. Bone's mechanostat: a 2003 update. Anatomical Record Part A Discoveries in Molecular Cellular & Evolutionary Biology 275, 1081.
13. Gleeson, P.B., Protas, E.J., Leblanc, A.D., Schneider, V.S., Evans, H.J., 1990. Effects of weight lifting on bone mineral density in premenopausal women. Journal of Bone & Mineral Research the Official Journal of the American Society for Bone & Mineral Research 5, 153.
14. Gotthardt, F., Huber, C., Thierfelder, C., Grize, L., Kraenzlin, M., Scheidegger, C., Meier, C., 2016. Bone mineral density and its determinants in men with opioid dependence. Journal of Bone & Mineral Metabolism, 1-9.
15. Harvey, N., Dennison, E., Cooper, C., 2014. Osteoporosis: A Lifecourse Approach. J Bone Miner Res 29, 1917-1925.
16. Heinonen, A., Sievänen, H., Kannus, P., Oja, P., Pasanen, M., Vuori, I., 2000. High-Impact Exercise and Bones of Growing Girls: A 9-Month Controlled Trial. Osteoporosis Int 11, 1010-1017.
17. Kay, A., Taylor, T.E., Barthwell, A.G., Wichelecki, J., Leopold, V., 2010. Substance Use and Women's Health. J Addict Dis 29, 139-163.
18. Kemmler, W., Von, S.S., 2011. Exercise and osteoporosis-related fractures: perspectives and recommendations of the sports and exercise scientist. Physician & Sportsmedicine 39, 142.
19. Khan, M., Cheung, A.M., Khan, A.A., 2017. Drug-Related Adverse Events of Osteoporosis Therapy. Endocrinology & Metabolism Clinics of North America 46, págs. 181-192.
20. Lejla K, Stephanie Z, Matthias N, et al. 2018. Associations Between Plasma Chemerin Concentrations and Bone Quality in Adults From the General Population. Endocrinology 159(6), 2378-2385.
21. Liu, J.M., Ma, L.Y., Bi, Y.F., Xu, Y., Huang, Y., Xu, M., Zhao, H.Y., Sun, L.H., Tao, B., Li, X.Y., Wang, W.Q., Ning, G., 2012. A Population-Based Study Examining Calcaneus Quantitative Ultrasound and Its Optimal Cut-Points to Discriminate Osteoporotic Fractures among 9352 Chinese Women and Men. J Clin Endocrinol Metab 97, 800-809.
22. Lynch, W.J., Peterson, A.B., Sanchez, V., Abel, J., Smith, M.A., 2013. Exercise as a novel treatment for drug addiction: a neurobiological and stage-dependent hypothesis. Neuroscience & Biobehavioral Reviews 37, 1622.
23. Mellon, S.J., Tanner, K.E., 2012. Bone and its adaptation to mechanical loading: a review. International Materials Reviews.
24. Milos, G., Gallo, L.M., Sosic, B., Uebelhart, D., Goerres, G., Haeuselmann, H.J., Eich, D., 2011. Bone Mineral Density in Young Women on Methadone Substitution. Calcif Tissue Int 89, 228-233.
25. Njeh, C.F., Boivin, C.M., Langton, C.M., 1997. The role of ultrasound in the assessment of osteoporosis: A review. Osteoporosis Int 7, 7-22.

26. Nordström, P., Sievänen, H., Gustafson, Y., Pedersen, N.L., Nordström, A., 2013. High physical fitness in young adulthood reduces the risk of fractures later in life in men: a nationwide cohort study. Journal of Bone & Mineral Research 28, 1061-1067.
27. Rodan, G.A., 1997. Bone mass homeostasis and bisphosphonate action. Bone 20, 1-4.
28. Senderovich H , Kosmopoulos A ,2018. An Insight into the Effect of Exercises on the Prevention of Osteoporosis and Associated Fractures in High-Risk Individuals. rambam maimonides medical journal 9(1).
29. Schiessl, H., Frost, H.M., Jee, W.S.S., 1998. Estrogen and bone-muscle strength and mass relationships. Bone 22, 1-6.
30. Smith, M.A., Schmidt, K.T., Iordanou, J.C., Mustroph, M.L., 2008. Aerobic exercise decreases the positive-reinforcing effects of cocaine. Drug Alcohol Depend 98, 129-135.
31. Tsuji, S., Haneda, M., Lee, C., Katsukawa, F., Onishi, S., Yamazaki, H., 1996. Effects of 3 months of non-weight-bearing cycle ergometric exercise on bone metabolism. Journal of bone and mineral metabolism 14, 21-25.
32. Tveit, M., Rosengren, B.E., Nilsson, J.Å., Karlsson, M.K., 2015. Exercise in youth: High bone mass, large bone size, and low fracture risk in old age. Scand J Med Sci Spor 25, 453.
33. Wang, M.C., Bachrach, L.K., Van Loan, M., Hudes, M., Flegal, K.M., Crawford, P.B., 2005. The relative contributions of lean tissue mass and fat mass to bone density in young women. Bone 37, 474-481.
34. Weaver C M , Gordon C M , Janz K F , et al. 2016. Erratum to: The National Osteoporosis Foundation’s position statement on peak bone mass development and lifestyle factors: a systematic review and implementation recommendations. Osteoporosis International 27(4), 1387-1387.
35. Wen, H.J., Huang, T.H., Li, T.L., Chong, P.N., Ang, B.S., 2016. Effects of short-term step aerobics exercise on bone metabolism and functional fitness in postmenopausal women with low bone mass. Osteoporosis Int 28, 1-9.
36. Wen, H.J., Huang, T.H., Li, T.L., Chong, P.N., Ang, B.S., 2017. Effects of short-term step aerobics exercise on bone metabolism and functional fitness in postmenopausal women with low bone mass. Osteoporosis Int 28, 539.