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Effects of Moderate- and High-Intensity Acute Aerobic Exercise on Food Reward and Appetite in Individuals with Methamphetamine Dependence

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Abstract

Purpose: Drug addiction is characterised by overvaluation of drug-related rewards and undervaluation of "natural", non-drug-related rewards. Methamphetamine (MA) is the second largest illegally abused drug in the world. Studies have shown that acute aerobic exercise can reduce the incidence of MA abusers' craving for drug-related cues, but the impact of exercise on food reward in this population has yet to be established. The aim of this study was to determine the effects of moderate and high-intensity acute aerobic exercise on food reward and subjective feelings of appetite in MA abusers.

Methods: Forty-four men, who met the DSM-V criteria for MA dependence, with BMI of 24.7±3.1 kg/m2 and age of 31.9±3.8 years, were randomly assigned to two exercise training groups: moderate- (n=22; 65%~75% HRmax) or high- (n=22; (>=85% HRmax) intensity. Each group performed a resting control or exercise session for 35 minutes, 1wk apart, in a counterbalanced order. Food reward (explicit liking, implicit wanting and relative preference) for high or low fat and sweet or savoury food images was assessed by the Leeds Food Preference Questionnaire and subjective feelings of appetite were measured by VAS.

Results: Greater relative preference (high: P=0.018; moderate: P=0.034) and implicit wanting (high: P=0.018; moderate: P=0.034) for high-fat savoury foods was noted following acute aerobic exercise compared to the control session. Exercise also increased subjective sensations of hunger (F (1,42) =8.28, P=0.006).

Conclusions: The current study provides the first evidence that acute aerobic exercise can increase reward for high fat savoury foods and stimulate appetite in MA-dependent individuals. In the context of exercise as a therapeutic option for MA dependence, these changes suggest an improvement in responsiveness to natural, non-drug rewards.

Keywords: aerobic exercise; food reward; methamphetamine abuser

1. Introduction

Drug addiction is a major public health problem worldwide, impacting significantly on the physical and mental health of abusers, facilitating the occurrence of a variety of criminal acts and placing a huge burden on the national economy in drug control and addiction treatment [1]. Worldwide, it is estimated that as many as 53.87 million people between the ages of 15 and 64 used amphetamine-type stimulants at least once in 2013 for non-medical purposes and methamphetamine (MA) has become the second largest illegally abused drug in the world after marijuana [2]. About two-thirds of the world's MA/amphetamine users live in east and southeast Asia [3] and methamphetamine dependence is rapidly increasing in China, almost 2.51 million registered patients suffer from methamphetamine dependence, which accounts for 60.5% of the total number of drug abusers [4]. Long-term use has been linked to repeated relapse episodes, possibly exacerbated by cognitive impairment during drug withdrawal [5].

Therefore, measures must be taken to diminish cognitive impairment during drug withdrawal. Addicted individuals become more responsive to drug cues and stressful stimuli, less responsive to natural rewards, and lose the flexibility to adjust the significance of rewards according to the situation [6]. One of the core manifestations of human substance dependence is a focus on finding and using drugs while neglecting activities unrelated to drugs [7]. This leads to the hypothesis that drug addiction in humans is associated with overestimation of drug-related rewards and underestimation of natural, non-drug-related rewards [8-10]. Consequently, it may be beneficial to reduce the value of drug-related rewards and improve the hedonic response to natural, non-drug rewards during withdrawal through cognitive behavioral or pharmacological intervention. At the same time, the hypothesis supports the potential utility of food reward procedures in clinical research in order to evaluate treatment outcomes for methamphetamine use disorder [11]. Food, as a potent natural reward, has been used to evaluate the sensitivity and functioning of the reward system in drug abusers [12-15].

Aerobic exercise is currently proposed as a potential treatment for substance abuse [16-18]. Studies have shown that exercise can reduce sensitivity to drug cues and subsequent drug intake [19]. Several animal studies have found that exposure to exercise reduces drug-related behaviours. For example, exercise has been shown to reduce self-administration of morphine, ethanol and cocaine in rats [20-23]. There is also evidence that exercise may "out-compete" drug self-administration, because when both reinforcers were concurrently available, wheel running reduced amphetamine intake in rats [24], Similarly, moderate intensity acute aerobic exercise was shown to reduce drug cravings in methamphetamine-dependent individuals and promoted inhibitory control over drug and non-drug-related cues [25, 26].

Since acute aerobic exercise appears to reduce MA-related cravings, it can be questioned whether these effects are accompanied by changes in food preference or food reward. There have been several investigations of the effect of acute exercise interventions on food reward. Exercise has been shown to impact on food reward in both normal weight [27] and overweight and obese [28, 29] subjects, after moderate [30] or high intensity [31] aerobic exercise.

Food "liking" (*i.e.* the acute sensory pleasure elicited by food) and food "wanting" (i.e. the objective, and sometimes implicit, motivation to seek and consume a target food) have previously been identified as major forces in guiding human eating behavior [32, 33]. In overweight and obese people, as well as those who exhibit binge eating, liking and wanting responses to high fat or fat-sweet foods are exaggerated, as opposed to drug addicts [34]. The Leeds Food Preference Questionnaire (LFPQ) has been shown to demonstrate reliable immediate post-exercise changes [35] and is a good predictor of food choice and intake in laboratory and community settings [36]. In addition to measuring relative food preferences, the instantiation of food reward in the LFPQ is conceptualized through separate “explicit liking” and “implicit wanting” responses to different categories of food according to fat content and sweet taste. This procedure has yet to be adapted for Chinese or drug-dependent individuals.

The objective of the current study was to examine the acute effects of moderate and high intensity aerobic exercise training in MA-dependent individuals on implicit wanting, explicit liking and relative preference for foods varying in fat content and taste. Subjective sensations of hunger, fullness and desire to eat were also taken post exercise to examine differences in appetite. Based on current literature, we hypothesized that there would be a dose-response effect of exercise intensity leading to increased liking and wanting for high fat and/or sweet foods relative to a non-exercise control condition in MA-dependent individuals.

2. Materials and Methods

2.1. Participants

44 males (ages: 31.9±3.8 years; BMI: 24.7 ± 3.1 kg/m^2) were recruited from the Drug Rehabilitation Bureau of the Shi Liping in Zhejiang province. Participants were included if they met the following criteria: (1) All the participants met the criteria for MA dependence according to the Structured Diagnostic Interview from the DSM-V, who were incarcerated and actively receiving detoxification treatment; (2) weight stable (<±3kg change over last 3 months); (3) aged 18~45 years; (4) no history of GI surgery or disorder, non-diabetic, no medical conditions and not taking medication known to influence gastric emptying or appetite.

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and the institutional Review Board of Shanghai University of Sport. Written informed consent was obtained from all participants before enrolling in the study.

2.2. Study Design

Seventy-three of 303 eligible participants were randomly assigned into either the Moderate or High intensity aerobic exercise group, and 44 participants completed the entire trial (figure 1). There were no significant differences between the Moderate (n=22) and High intensity (n=22) exercise groups in age, BMI, cardiovascular fitness (resting heart rate) or history of MA use prior to the exercise intervention (table 1). Each group completed testing at baseline and post-exercise or rest, 1 week apart and in a counterbalanced order. During the preliminary session, anthropometric data were collected, participants were asked not to do strenuous exercise or drink alcohol for 24 hours prior to testing. Eating or drinking caloric or caffeinated beverages was forbidden two hours prior to testing.

	Total		Moderate		High		t-test
	Mean	SD	Mean	SD	Mean	SD	
Demographic							
Age (year)	31.9	3.8	31.2	3.3	32.6	4.2	0.22
Height (m)	1.7	0.1	1.7	0.1	1.7	0.1	0.67
Weight (kg)	71.7	10.1	71.4	9.9	71.9	10.5	0.86
Fitness							
BMI (kg/m2)	24.7	3.1	24.6	3.1	24.9	3.1	0.71
Basal heart rate (time/min)	74.2	8.0	74.1	7.4	74.2	8.7	0.97
MA data							
Duration (years)	6.9	2.9	6.5	3.3	7.4	2.4	0.30
Usage (gram/time)	0.4	0.5	0.4	0.7	0.3	0.3	0.58
Frequency (day/wk)	2.8	2.7	2.3	2.3	3.2	2.9	0.29

Table 1. Details of the anthropometric information in all participants and the comparison between the two groups.

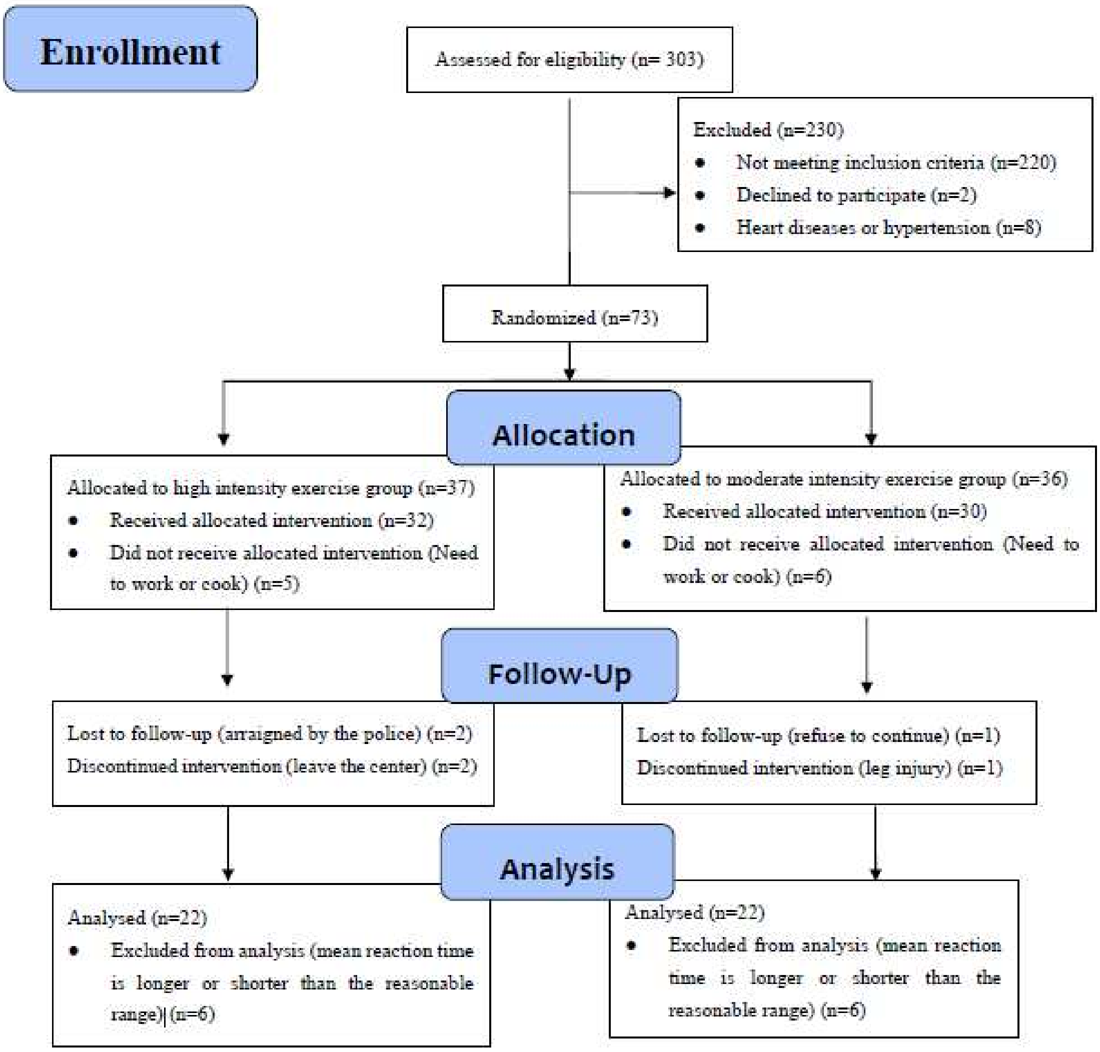

Figure 1. Flowchart of participant enrollment in the study.

2.3. Food Reward Assessment

Participants completed the Leeds Food Preference Questionnaire (LFPQ) [37], a validated computer-based behavioural procedure administered using experiment software (E-prime v.2.0, Psychology Software Tools, ND), which was adapted and translated into Chinese. The original LFPQ was translated into Chinese by one of the authors (ZY) who is a Chinese native speaker. The translation was discussed with co-author and developer of the original LFPQ (GF) and reviewed and confirmed by a teacher of English as a second language from the staff of University of Nanjing. In addition, a culturally appropriate set of 50 food images were selected from the paid photo gallery website for use in Chinese (www.xxxxx.com). Ratings of the foods' intensity of sweet taste (none-high), and the perceived fat content (low-high) were rated using 7-point Likert scales. The average means of participants' responses were compared with the reference mean using one-sample t-test, and the reference mean was determined as 6 for the high content of sweet and fat, and 2 for the low content of sweet and fat. The final four food images selected for each category were taken from the outcome of these results and are shown in Table 2.

Briefly, the LFPQ provides measures of implicit wanting, explicit liking and relative preference for an array of food images, varying along dimensions of fat content and sweet taste. A total of 16 different foods, divided into four categories (high-fat savoury, low-fat savoury, high-fat sweet and low-fat sweet) formed the array for this study.

Sweet		Savoury	
High fat	Low fat	High fat	Low fat
Ice-cream	Popcorn	Hamburger	Cucumber
Cream cake	Juice	Marble meat	Salad
Chocolate	Marshmallow	Pizza	Vegetables
Donuts	Mixed fruits	Chips (fries)	Bread

Table 2. Photographic food stimuli used in the computer task (grouped by food category)

2.3.1. Implicit Wanting and Relative Preference

In a forced-choice paradigm, each food image was randomly presented with every other image in a series of food pair trials. The participants were instructed to select the food they "most want to eat now" before each trial. The parameters were set as 96 randomized food pair trials presented and each stimulus appearing 12 times. Stimuli were presented until a valid response was detected up to a maximum of 4000ms with a 500ms washout between presentations in which a central fixation cross was displayed. A standardized implicit wanting score for each food category was calculated as a function of the mean reaction time in selecting a food category adjusted for the frequency of choice for each category [34]. A positive score on the implicit wanting measure indicates a more rapid selection for a given food category relative to the alternatives in the task and a negative score indicates the opposite. In addition, the frequency of selections made in each category (with a possible range of 0–48) was measured which reveals a relative preference among the food categories.

2.3.2. Explicit liking

Explicit liking for the same images and categories in the forced-choice task was measured from the 16 food stimuli presented one at a time and rated according to a 100-mm VAS anchored at each end by the statements "not at all" and "extremely". Subjects were prompted with the statement "How pleasant would it be to experience a mouthful of this food now?" The VAS was presented on-screen beneath each food stimulus and subjects used the mouse to move a centred cursor along the line to indicate their response. When a rating was made, the procedure automatically cycled to the next stimulus trial in a randomized order.

2.4. Subjective Appetite Sensations

Subjective appetite sensations were measured immediately after exercise or reading using visual analogue scales on an electronic appetite rating system [38]. Participants were asked to rate feelings of hunger, fullness and desire to eat on 100 mm visual analogue scales, anchored at each end with the statements "not at all" and "extremely".

2.5. Exercise Protocol

The aerobic exercise was performed using a bicycle ergometer (SH-5000U) at 50 rpm and involved a 5-min warm-up, a 25-min main exercise period, and a 5-min cool-down. During the main exercise, the participant was instructed to cycle while keeping their heart rate at one of two exercise intensities, i.e., within the range of 65~75% or >=85% of their estimated maximum heart rate (206.9–0.67 × age) [39]. Heart rate was monitored using a Suunto smart sensor (Suunto Oy, Vantaa, Finland). The participants in the control group were required to read about drug abuse treatments, including exercise- and fitness-related information, in a quiet room for 35 min.

2.6. Statistical analysis

Statistical analyses were performed using IBM SPSS for Windows (Chicago, Illinois, Version 20). Two-way repeated measures ANOVA were used to determine the main effects of exercise intervention (Control and Exercise) and exercise intensity (Moderate and High) on food reward and appetite measures. Post hoc tests with Bonferroni adjustments were used to determine where significant differences existed. Values are presented as means ± standard deviations unless otherwise stated. Differences with P-values < 0.05 were considered statistically significant.

3. Results

3.1. Food reward

Firstly, on the three measures of relative preference, explicit liking and implicit wanting, the order of subjects' preference for the food categories was HFSA> HFSW> LFSW> LFSA (table 3). Independent of the exercise intervention, the high intensity group showed higher scores for LFSW foods compared to the moderate intensity group (P<0.025). On comparison of the food reward measures after exercise compared to rest, the ANOVA showed that exercise regardless of intensity resulted in a greater relative preference (moderate: P=0.034; high: P=0.018, figure 2A) and implicit wanting (high: P=0.017; moderate: P=0.044, figure 2B) for HFSA. No other significant differences between exercise compared to control, intensity, or interactions between exercise and intensity were noted in the food reward variables for any food category (see table 3). Therefore, acute aerobic moderate and high intensity exercise both appeared to increase the relative preference and implicit wanting for high-fat savoury foods compared to rest.

A

Relative preference	**Moderate**		**High**		**Exercise effect**	**Intensity effect**	**Exercise×Intensity effect**
	Mean	**SD**	**Mean**	**SD**			
HFSW							
Control	26.7	7.5	26.3	9.1	F=1.59	F=0.72	F=1.59
Exercise	26.0	9.1	22.5	8.2	P=0.214	P=0.401	P=0.214
HFSA							
Control	36.0	6.1	33.5	8.8	F=10.83	F=1.27	F=0.02
Exercise	38.7	5.9	36.4	7.9	**P=0.002**	P=0.266	P=0.881
LFSW							
Control	18.7	8.2	22.8	6.5	F=0.06	F=8.12	F=1.16
Exercise	17.3	6.6	23.6	5.4	P=0.816	**P=0.007**	P=0.288
LFSA							
Control	16.3	6.3	15.5	7.7	F=0.65	F=1.14	F=0.03

Exercise	15.3	6.2	14.8	7.3	P=0.426	P=0.709	P=0.859

B

Implicit wanting	Moderate		High		Exercise effect	Intensity effect	Exercise×Intensity effect
	Mean	SD	Mean	SD			
HFSW							
Control	5.6	16.6	6.6	21.7	F=2.6	F=0.56	F=2.1
Exercise	4.9	23.2	-4.0	20.4	P=0.112	P=0.458	P=0.158
HFSA							
Control	35.4	18.8	24.9	22.7	F=10.51	F=2.82	F=0.05
Exercise	43.3	14.2	34.0	21.8	**P=0.003**	P=0.102	P=0.828
LFSW							
Control	-16.8	20.2	-7.1	19.7	F=0.05	F=5.38	F=0.64
Exercise	-18.3	19.7	-4.3	16.9	P=0.825	**P=0.025**	P=0.427
LFSA							
Control	-21.3	16.6	-21.7	16.0	F=0.97	F=0.01	F=0.08
Exercise	-24.9	18.5	-23.7	18.6	P=0.330	P=0.932	P=0.785

C

Explicit liking	Moderate		High		Exercise effect	Intensity effect	Exercise×Intensity effect
	Mean	SD	Mean	SD			
HFSW							
Control	56.4	17.6	65.0	16.2	F=0.76	F=1.08	F=2.85
Exercise	58.3	15.7	59.2	17.6	P=0.390	P=0.306	P=0.099
HFSA							
Control	63.1	20.1	68.3	19.0	F=0.08	F=0.36	F=0.92
Exercise	66.2	11.2	66.5	17.5	P=0.786	P=0.551	P=0.342
LFSW							
Control	52.7	16.7	62.1	8.8	F=0.40	F=7.20	F=0.02
Exercise	51.7	10.8	60.5	14.1	P=0.533	**P=0.011**	P=0.903
LFSA							
Control	48.7	14.9	52.1	14.4	F=0.75	F=0.07	F=1.39
Exercise	49.4	11.4	47.9	9.3	P=0.391	P=0.787	P=0.246

Table 3. The relative preference (A), implicit wanting (B) and explicit liking (C) for high-fat sweet (HFSW), high-fat savoury (HFSA), low-fat sweet (LFSW) and low-fat savoury (LFSA) foods between exercise conditions (exercise and control), exercise intensity (moderate and high).

A B

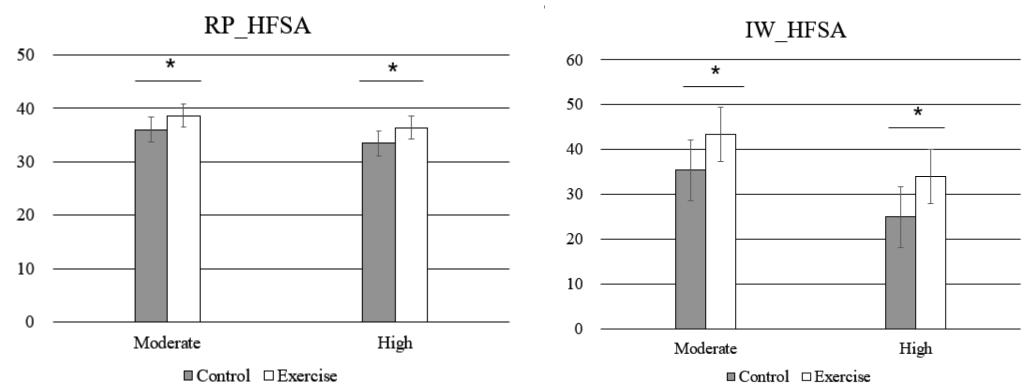

Figure 2. Relative preference and implicit wanting for high-fat savoury foods between exercise conditions grouped by exercise intensity. After both intensities of exercise, the relative preference and implicit wanting are significantly increased. Values are presented as means for participants with standard errors of the mean represented by vertical bars. HFSA, high fat savoury; RP, relative preference; IW, implicit wanting. *P<0.05.

3.2.Subjective sensations of appetite

Subjective feelings of appetite, in terms of hunger, fullness and desire to eat after exercise and control sessions are shown in table 4. There was a higher mean rating of hunger after high intensity exercise compared to moderate intensity (figure 3), but no main effect of exercise intensity or interaction effect. No significant effect of exercise, intensity or interaction was observed for subjective feelings of fullness or desire to eat.

	Moderate		**High**		**Intensity effect**	**Exercise effect**	**Exercise×Intensity effect**
	Mean	**SD**	**Mean**	**SD**			
Desire							
Control	48.99	29.8	54.91	34.675	F(1,42)=0.09	F(1,42)=0.75	F(1,42)=0.44
Exercise	54.11	27.06	52.82	27.658	P=0.766	P=0.748	P=0.444
Fullness							
Control	54.7	27.13	48.41	30.844	F(1,42)=0.10	*F(1,42)*=0.05	F(1,42)=1.30
Exercise	49.81	21.89	51.73	22.455	P=0.754	P=0.829	P=0.260
Hunger							
Control	35.24	25.55	37.8	32.675	F(1,42)=0.45	F(1,42)=8.28	F(1,42)=0.57
Exercise	43.93	28.12	52.66	25.172	P=0.450	***P*=0.006**	P=0.456

Table 4. Fasting subjective appetite sensations after high or moderate intensity exercise and control sessions. SD, standard deviation.

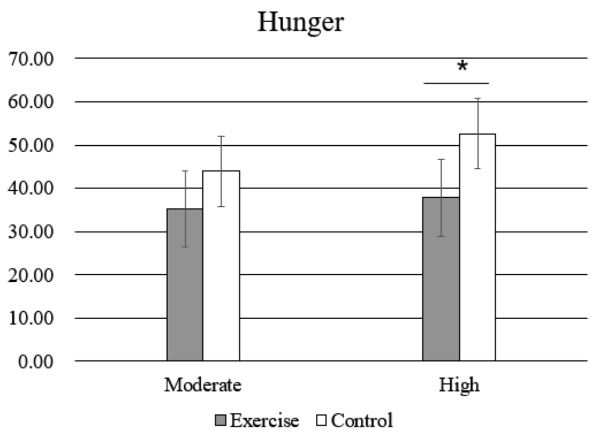

Figure 3. Subjective feeling of hunger after moderate or high intensity exercise and rest. *P<0.05.

4. Discussion

This study examined the acute effects of moderate and high intensity aerobic exercise on food reward and appetite in individuals with methamphetamine dependence. In partial support of our hypotheses, the findings showed that the relative preference and implicit wanting for high-fat savoury foods increased following exercise compared to rest, but that this was independent of exercise intensity. Furthermore, high intensity exercise significantly increased subjective feelings of hunger, compared to the resting control session.

Contrary to our prediction, MA-independent people showed no change in preference, liking or wanting for sweet food. In opiate users, previous research has reported strong craving, preference for, and intake of sugary foodstuffs either when maintained on opiate agonists or when abstinent [40-42]. Moreover, changes in taste perception may underlie altered consumption of refined sugars in opiate users [10]. In the present study, only changes in the immediate reward value of high-fat savoury food was noted. The reason for the absence of an increase or decrease in liking or wanting for sweet taste foods could be that sweet taste preference is not diminished in drug addicts. Indeed, preference for sweetened water over cocaine has been shown in rats, even in animals with a history of drug intake [43]. In the present study, HFSA foods were the highest category on all measures of food reward after exercise and rest. Consequently, the observed increase in wanting and preference for HFSA may be due the relatively high reward value of this category of food in these individuals. In healthy individuals, one study found that a single bout of aerobic or resistance exercise led to a decrease in neuronal activity in brain regions associated with food reward (insula, orbitofrontal cortex, putamen) [31], which is opposite to this study. Furthermore, in healthy non-obese adults, acute aerobic exercise tends to reduce subjective feelings of hunger [31], which is contrary to the present finding in MA addicts.

The increase in subjective hunger, relative preference and implicit wanting for high-fat savoury foods may be altogether indicative of an increase in the natural motivation to eat in this clinical population. Preclinical drug versus food choice procedures have been used for years to evaluate pharmacotherapy candidates for drug dependence, such as cocaine [44] and heroin [45], however, the use of food choice paradigms in evaluating the drug development process in methamphetamine abuse has only occurred in recent years. The present findings suggest that the assessment of food reward and appetite in the treatment of MA dependence could be beneficial as a clinical endpoint.

There are a number of limitations to consider in the evaluation of this study. Firstly, our experiment was conducted in a drug rehabilitation center, with many practical and ethical restrictions over access to patients. Therefore, it was not possible to administer test meals or measure food intake to assess the translation between the results of food reward in MA dependent individuals to their actual eating behavior. Secondly, we opted for a between-subjects design to compare exercise intensities to shorten the duration of the study. A within-subjects design may have been more sensitive to reveal dose-dependent effects of intensity, and only a single rating of hunger was taken at the end of each condition. Hunger ratings before and after the exercise/rest and for a period afterwards would be stronger for the measurement of subjective appetite. Thirdly, no healthy control or non MA-dependent individuals were recruited into the trial to compare with the MA-dependent sample and this should be addressed in future research seeking to extend these findings. Finally, the standard deviation of the experimental results was relatively large, indicating that further studies with bigger sample sizes may be needed to confirm these results.

This randomized controlled trial found that 35 minutes of acute aerobic exercise can affect food reward in MA-dependent individuals by increasing implicit wanting and preference for high fat savoury foods and increasing post-exercise levels of hunger. These changes offer preliminary evidence that may indicate a beneficial therapeutic response to exercise with the normalization of appetite and natural food reward in place of the reward for drugs of abuse in this population. In future research it would be useful to examine different modalities, duration and intensities of exercise, in combination with more detailed assessment of eating behaviour under laboratory and free-living situations. Furthermore, more detailed assessments should be taken alongside food reward, such as neurological and hormonal indicators. Secondly, the measurement of food and drug reward should be combined to provide a reliable indicator of the withdrawal status of drug addicts. Finally, because the neuropharmacological effects of different dependent drugs on the brain are different, the degree of damage to cognitive function are also different. For example, transition to addiction is faster after exposure to methamphetamine compared to marijuana [6]. As a result, this research should be extended to other types of drug dependence and other therapeutic interventions in the future.

To conclude, the present study reports the novel finding that acute aerobic exercise may improve food reward and appetite response in MA-dependent individuals. Combined with previous research demonstrating that acute aerobic exercise can reduce cravings for MA, the present findings support the notion that exercise could be used as a therapeutic intervention to restore the balance between drug and non-drug rewards. Our preliminary findings warrant future studies to explore the potential role of chronic aerobic exercise in facilitating MA withdrawal.

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